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glucose and **glucagon** in the relatives were not different from those in the controls. We conclude that elevated fasting PIM levels in patients with **type 2 diabetes** seem not to be a genetic trait. First-degree relatives of patients with **type 2 diabetes** are truly hyperinsulinemic in the fasting state, and they have proportional PIM, insulin and C-peptide responses to glucose and **glucagon**.

search notes

3/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009093974 BIOSIS NO.: 199497115259
Effect of **glucagon**-like peptide 1 on glucose turnover in normal man
AUTHOR: Holst J J (Reprint); Hvidberg A; Nielsen M Toft; Hilsted J; Orskov C
AUTHOR ADDRESS: Dep. Med. Physiol., Panum Inst., Copenhagen, Denmark** Denmark
JOURNAL: Digestion 54 (6): p383-384 1993 **1993**
CONFERENCE/MEETING: International Symposium on Glucagon-Like Peptide-1 Copenhagen, Denmark May 17-19, 1993; 19930517
ISSN: 0012-2823
DOCUMENT TYPE: Meeting; Abstracts Only
RECORD TYPE: Citation
LANGUAGE: English

3/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009093955 BIOSIS NO.: 199497115240
Glucagon-like peptide 1(7-37) and glibenclamide stimulate insulin secretion and biosynthesis by different glucose-dependent mechanisms: Comparison in vivo and in vitro
AUTHOR: Parker Janice C (Reprint); Hargrove Diane M; Shepherd Kandace L; Nardone Nancy A; Andrews Kim M; Persson Lorna M
AUTHOR ADDRESS: Central Res. Div., Pfizer Inc., Groton, CT 06340, USA**USA
JOURNAL: Digestion 54 (6): p357-358 1993 **1993**
CONFERENCE/MEETING: International Symposium on Glucagon-Like Peptide-1 Copenhagen, Denmark May 17-19, 1993; 19930517
ISSN: 0012-2823
DOCUMENT TYPE: Meeting; Abstracts Only
RECORD TYPE: Citation
LANGUAGE: English
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Set	Items	Description
S1	5715	GLUCAGON AND (TYPE(W)2 OR TYPE(W)II OR NIDDM) AND DIABETES
S2	1360	S1 AND PY<1994
S3	765	RD S2 (unique items)

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insulin-induced hypoglycemia in 10 **NIDDM** patients without autonomic neuropathy and in 6 age- and weight-matched normal controls. Recovery of plasma glucose concentration and hypoglycemia-induced increments of plasma concentrations of **glucagon**, epinephrine, norepinephrine, and HGH were similar in the **NIDDM** patients and the age- and weight-matched nondiabetic controls. It appears likely, therefore, that these **NIDDM** patients, if **treated** aggressively with insulin, may be at lesser risk for severe and prolonged hypoglycemia than insulin-dependent diabetic patients, particularly those with autonomic neuropathy or those **treated** with beta-adrenergic antagonists.

5/7/140 (Item 53 from file: 73)
DIALOG(R)File 73:EMBASE

02769128 EMBASE No: 1984038087
Present situation of **treatment** with biguanide derivatives: metformin
AKTUELLER STAND DER THERAPIE MIT BIGUANIDEN (METFORMIN)
Knick B.; Knick J.; Groth U.; Panitz N.
Fachbereich Diabetologie, Stiftung Deutsche Klinik fur Diagnostik, 6200 Wiesbaden Germany
Therapiewoche (THERAPIEWOCHE) (Germany) 1983, 33/50 (6764-6775)
CODEN: THEWA
DOCUMENT TYPE: Journal
LANGUAGE: GERMAN SUMMARY LANGUAGE: ENGLISH

The mode of action and the side effects of biguanides have been elucidated by modern techniques in the last decennium. Metformin is an antidiabetic substance which is well tolerated considering the contraindications. In addition to the inhibition of the Krebs cycle an increase of the number of insulin receptors and a suppression of the postprandial **glucagon** level have been demonstrated. The clinical indications for metformin are currently the following: 1. Monotherapy with metformin for **type II diabetes** in overweight dietetically not correctly **treated** for further weight reduction. 2. Metformin-sulfonylurea combination therapy for the so-callded 'SH medication secondary failure'. 3. Metformin-insulin combination therapy for the insulin dependent **type II** diabetic with still residual non-sufficient insulin reserve. Considering the contraindications, the therapeutic advantages of metformin **treatment** can be used for the **type II** diabetic.

5/7/141 (Item 54 from file: 73)
DIALOG(R)File 73:EMBASE

02700083 EMBASE No: 1984119042
Insulin secretion in **type II** diabetics: **In vivo** and in vitro investigation
Verlohren H.-J.; Jahr H.
Municipal Hospital of Internal Medicine, GDR-7033 Leipzig Germany
Experimental and Clinical Endocrinology (EXP. CLIN. ENDOCRINOL.) (Germany) 1984, 83/2 (216-224)
CODEN: EXCED
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

Many cases of **type II diabetes** present an anomaly of insulin secretion which is characterized by a missing, reduced, or delayed

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3/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009182737 BIOSIS NO.: 199497204022
Pseudo **type II diabetes** (latent insulin-dependent **diabetes** mellitus): Clinical, biochemical, immunogenetic and immunological parameters
AUTHOR: Scherbaum W A
AUTHOR ADDRESS: Dep. Endocrinol. Metabolism, Univ. Leipzig, Germany** Germany
JOURNAL: Zeitschrift fuer Rheumatologie 52 (6): p424 1993 **1993**
CONFERENCE/MEETING: Symposium on Autoimmune Diseases and Recombinant DNA-Technology Freiburg, Germany November 21-23, 1993; 19931121
ISSN: 0340-1855
DOCUMENT TYPE: Meeting; Abstracts Only
RECORD TYPE: Citation
LANGUAGE: English

3/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009149987 BIOSIS NO.: 199497171272
Plasma **glucagon** responses to insulin-induced hypoglycemia and arginine in spontaneous non-insulin-dependent **diabetes** mellitus (**NIDDM**) rats, Otsuka long evans Tokushima fatty (OLETF) strain
AUTHOR: Ishida Kaori; Mizuno Akira; Sano Toshiaki; Shi Keju; Shima Kenji (Reprint)
AUTHOR ADDRESS: Dep. Lab. Med., Sch. Med., Univ. Tokushima, 3-8-15 Kuramoto-Cho, Tokushima 770, Japan**Japan
JOURNAL: Acta Endocrinologica 129 (6): p585-593 1993 **1993**
ISSN: 0001-5598
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Pancreatic A-cell function in the newly developed Otsuka Long Evans Tokushima Fatty (OLETF) strain of non-insulin-dependent **diabetes** mellitus (**NIDDM**) rats was examined in relation to the morphological changes in their islets and the plasma **glucagon** responses to insulin-induced hypoglycemia and an arginine test by chronological studies in seven male OLETF and seven male non-diabetic control Long Evans Tokushima Otsuka (LETO) rats each at 10, 16 and 24 weeks of age and eight male OLETF rats that were placed in a cage with a wheel for exercising from 5 to 24 weeks of age. The hormonal contents and

morphological features of the pancreas of these rats were examined. After iv injection of insulin, the plasma **glucagon** level rose significantly from the basal level in OLETF rats at 10 weeks old, but little if at all in those of 16 and 24 weeks old. The pancreatic A cells of LETO rats of all age groups responded equally well to glucopenia. The areas under the response curves of plasma **glucagon** (SIGMA-DELTA-IRG) during the 90 min of insulin-induced hypoglycemia were 14496+-7860 vs 9588+-3930, 2257+-3018 vs 9235+-5447 (p lt 0.05) and 826+-985 vs 9707+-2510 (p lt 0.01) ng cntdot min-1 cntdot l-1 in OLETF rats vs LETO rats of 10, 16 and 24 weeks old, respectively. The plasma **glucagon** responses during the arginine test were higher in OLETF rats than in LETO rats at 10 and 16 weeks but not at 24 weeks of age. Exercise-trained OLETF rats of 24 weeks old had normal ability to secrete **glucagon** from the pancreas in response to glycopenia (SIGMA-DELTA-IRG: 8645+-2467 ng cntdot min-1 cntdot l-1). There were no significant differences in on the pancreas of sedentary OLETF rats of 24 weeks old revealed enlarged, multilobulate, fibrotic islets in which A cells did not occupy a peripheral position but were widely dispersed, whereas in sections of the islets from exercise-trained rats the microstructure and locations of A and B cells appeared normal. These results demonstrated that the pancreatic A-cell response to glucopenia was impaired in old sedentary OLETF rats, probably due to an abnormal A-cell-B-cell morphofunctional relationship.

3/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009103710 BIOSIS NO.: 199497124995
Proportional proinsulin responses in first-degree relatives of patients with **type 2 diabetes** mellitus
AUTHOR: Roder M E (Reprint); Eriksson J; Hartling S G; Groop L; Binder C
AUTHOR ADDRESS: Div. Endocrinology Metabolism, VA Med. Cent., 1660 South Columbian Way, Seattle, WA 98108, USA**USA
JOURNAL: Acta Diabetologica 30 (3): p132-137 1993 **1993**
ISSN: 0940-5429
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Elevated fasting proinsulin immunoreactive material (PIM) has previously been found in patients with **type 2** (non-insulin-dependent) **diabetes** mellitus. It is not known whether this is a genetic trait or whether it is related to the manifestation of **type 2 diabetes**. Neither is it clear whether the raised fasting insulin immunoreactivity previously observed in first-degree relatives of patients with **type 2 diabetes** is due to raised PIM. Furthermore, it has not been investigated whether first-degree relatives have altered PIM responses to different secretagogoues. To study this, PIM, insulin and C-peptide were measured in patients with **type 2 diabetes**, in their first-degree relatives and in healthy control subjects in the fasting state and in relatives and controls during a hyperglycemic clamp. At the end of the hyperglycemic clamp, 0.5 mg of **glucagon** was given intravenously to stress the beta cells further. Fasting PIM concentrations were significantly higher in patients with **type 2 diabetes** (P lt 0.05). These patients did not have significantly elevated fasting insulin levels when corrected for PIM. In the relatives, fasting insulin concentrations were elevated but PIM levels were normal suggesting that the increase in fasting insulin concentrations reflected an increase in true insulin. The incremental PIM, insulin and C-peptide responses to

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4/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009093955 BIOSIS NO.: 199497115240
Glucagon-like peptide 1(7-37) and glibenclamide stimulate insulin secretion and biosynthesis by different glucose-dependent mechanisms: Comparison **in vivo** and in vitro
AUTHOR: Parker Janice C (Reprint); Hargrove Diane M; Shepherd Kandace L; Nardone Nancy A; Andrews Kim M; Persson Lorna M
AUTHOR ADDRESS: Central Res. Div., Pfizer Inc., Groton, CT 06340, USA**USA
JOURNAL: Digestion 54 (6): p357-358 1993 **1993**
CONFERENCE/MEETING: International Symposium on Glucagon-Like Peptide-1 Copenhagen, Denmark May 17-19, 1993; 19930517
ISSN: 0012-2823
DOCUMENT TYPE: Meeting; Abstracts Only
RECORD TYPE: Citation
LANGUAGE: English

4/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0009009260 BIOSIS NO.: 199497030545
Rapid publications: Cloning and functional expression of the human islet GLP-1 receptor. Demonstration that exendin-4 is an agonist and exendin-(9-39) an antagonist of the receptor
AUTHOR: Thorens Bernard (Reprint); Porret Andree; Buehler Leo; Deng Shao-Ping; Morel Philippe; Widmann Christian
AUTHOR ADDRESS: Inst. Pharmacol. Toxicol., 27 Bugnon, 1005 Lausanne, Switzerland**Switzerland
JOURNAL: Diabetes 42 (11): p1678-1682 1993 **1993**
ISSN: 0012-1797
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A complementary DNA for a **glucagon**-like peptide-1 receptor was isolated from a human pancreatic islet cDNA library. The isolated

clone encoded a protein with 90% identity to the rat receptor. In stably transfected fibroblasts, the receptor bound (125I)GLP-1 with high affinity (K-d = 0.5 nM) and was coupled to adenylate cyclase as detected by a GLP-1-dependent increase in cAMP production (EC-50 = 93 pM). Two peptides from the venom of the lizard Heloderma suspectum, exendin-4 and exendin-(9-39), displayed similar ligand binding affinities to the human GLP-1 receptor. Whereas exendin-4 acted as an agonist of the receptor, inducing cAMP formation, exendin-(9-39) was an antagonist of the receptor, inhibiting GLP-1-induced cAMP production. Because GLP-1 has been proposed as a potential agent for **treatment** of **NIDDM**, our present data will contribute to the characterization of the receptor binding site and the development of new agonists of this receptor.

4/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008821245 BIOSIS NO.: 199395123511
Acipimox increases glucose disposal in normal man independent of changes in plasma nonesterified fatty acid concentration and whole-body lipid oxidation rate
AUTHOR: Fulcher G R (Reprint); Walker M; Farrer M; Johnson A S; Alberti K G M M
AUTHOR ADDRESS: Dep. Endocrinology, Royal North Shore Hospital, Pacific Highway, St. Leonards, 2065 Sydney, NSW, Australia**Australia
JOURNAL: Metabolism Clinical and Experimental 42 (3): p308-314 **1993**
ISSN: 0026-0495
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The short-term administration of a nicotinic acid analogue (acipimox) increases insulin sensitivity and consequently glucose disposal, both in patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) and in patients with cirrhosis. This effect has been attributed to a decrease in plasma nonesterified fatty acid (NEFA) levels and fatty acid oxidation rates, and a corresponding increase in carbohydrate oxidation. The aim of the present study was to determine whether acipimox influenced glucose disposal independent of changes in lipid metabolism. Seven normal men (age, 31 +- 4 years; body mass index, 23.2 +- 1.8 kg cntdot m-2; fat-free mass (FFM), 66.8 +- 4.2 kg) were studied on two separate occasions with hyperinsulinemic (0.06 U cntdot kg FFM-1 cntdot h-1) euglycemic clamps (duration, 150 minutes). A primed (150 U), continuous (0.4 U cntdot kg-1 cntdot min-1) infusion of heparin together with 10% intralipid (25 mL cntdot h-1) was infused in both studies from -90 to 150 minutes to maintain comparable levels of plasma NEFA and lipid oxidation rates. Acipimox (500-mg capsules) or placebo were **administered** orally in a double-blind random fashion at t = -90 and t = 0 minutes. Whole-body lipid and carbohydrate oxidation were measured in the last 30 minutes of both the basal (preclamp) period (-30 to 0 minutes) and the clamp period (120 to 150 minutes). Mean plasma NEFA concentrations were similar throughout both studies (-90 to 0 minutes, 0.84 +- 0.08 v 0.85 +- 0.11 mmol cntdot L-1; 30 to 60 minutes, 0.58 +- 0.03 v 0.58 +- 0.03 mmol cntdot L-1; 120 to 150 minutes, 0.48 +- 0.05 v 0.51 +- 0.11 mmol cntdot L-1; all NS), as were whole-body lipid oxidation rates (-30 to 0 minutes acipimox v placebo 0.71 +- 0.11 v 0.69 +- 0.07 mg cntdot kg FFM-1 cntdot min-1, NS; 120 to 150 minutes, 0.17 +- 0.07 v 0.21 +- 0.07 mg cntdot kg FFM-1 cntdot min-1, NS). Steady-state mean blood glucose levels were the same (120 to 150 minutes, 4.3 +- 0.2 v 4.3 +- 0.1 mmol cntdot L-1). Despite this, there was a significant increase in glucose disposal following acipimox **treatment** (9.00 +- 0.8 v 7.96

+- 0.8 mg cntdot kg FFM-1 cntdot min-1, P lt .01), which could be attributed to a significant increase in nonoxidative glucose disposal (5.36 +- 0.81 v 4.36 +- 0.64 mg cntdot kg FFM-1 cntdot min-1, P = .01). These data suggest that acipimox has a direct (pharmacological) effect on glucose disposal that is not mediated through changes in plasma NEFA concentrations or total-body lipid oxidation rates.

4/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008810197 BIOSIS NO.: 199395112463
Pancreatic beta-cells are rendered glucose-competent by the insulinotropic hormone **glucagon**-like peptide-1(7-37)
AUTHOR: Holv George G Iv (Reprint); Kuhtreiber Willem M; Habener Joel F (Reprint)
AUTHOR ADDRESS: Lab. Mol. Endocrinol., Mass. Gen. Hosp., Howard Hughes Medical Inst., Harvard Medical Sch., Boston, MA 02114, USA**USA
JOURNAL: Nature (London) 361 (6410): p362-365 **1993**
ISSN: 0028-0836
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Non-insulin-dependent **diabetes** mellitus (**NIDDM, type 2 diabetes**) is a disorder of glucose homeostasis characterized by hyperglycaemia, peripheral insulin resistance, impaired hepatic glucose metabolism, and diminished glucose-dependent secretion of insulin from pancreatic beta-cells-1. **Glucagon**-like-peptide-1(7-37) (GLP-1)-2 is an intestinally derived hormone that may be useful for the **treatment** of **NIDDM** because it acts **in vivo** to increase the level of circulating insulin, and thus lower the concentration of blood glucose-3,4. This therapeutic effect may result from the ability of GLP-1 to compensate for a defect in the glucose signalling pathway that regulates insulin secretion from beta-cells. In support of this concept we report here that GLP-1 confers glucose sensitivity to glucose resistant beta-cells, a phenomenon we term glucose competence. Induction of glucose competence by GLP-1 results from its synergistic interaction with glucose to inhibit metabolically regulated potassium channels that are also targeted for inhibition by sulphonylurea drugs commonly used in the **treatment** of **NIDDM**-5. Glucose competence allows membrane depolarization, the generation of action potentials, and Ca-2+ influx, events that are known to trigger insulin secretion-6.7.

4/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008793379 BIOSIS NO.: 199395095645
Preserved incretin activity of **glucagon**-like peptide-1 (7-36-amide) but not of synthetic human gastric inhibitory polypeptide in patients with **type-2 diabetes** mellitus
AUTHOR: Nauck Michael A (Reprint); Heimesaat Markus M; Orskov Catherine; Holst Jens J; Ebert Reinhold; Creutzfeldt Werner
AUTHOR ADDRESS: Gastroenterol. and Endocrinol., Dep. Intern Med., Georg-August-Universitaet, Robert-Koch-Strasse 40, D-3400 Goettigen, Germany**Germany
JOURNAL: Journal of Clinical Investigation 91 (1): p301-307 **1993**
ISSN: 0021-9738

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In **type-2 diabetes**, the overall incretin effect is reduced. The present investigation was designed to compare insulinotropic actions of exogenous incretin hormones (gastric inhibitory peptide (GIP) and **glucagon**-like peptide 1 (GLP-1) (7-36-amide)) in nine **type-2** diabetic patients (fasting plasma glucose 7.8 mmol/liter; hemoglobin A-1c 6.3+-0.6%) and in nine age- and weight-matched normal subjects. Synthetic human GIP (0.8 and 2.4 pmol/kg cntdot min over 1 h each), GLP-1(7-36-amide) (0.4 and 1.2 pmol/kg cntdot min over 1 h each), and placebo were **administered** under hyperglycemic clamp conditions (8.75 mmol/liter) in separate experiments. Plasma GIP and GLP-1 (7-36-amide) concentrations (radioimmunoassay) were comparable to those after oral glucose with the low, and clearly supraphysiological with the high infusion rates. Both GIP and GLP-1 (7-36 amide) dose-dependently augmented insulin secretion (insulin, C-peptide) in both groups (P lt 0.05). With GIP, the maximum effect in **type-2** diabetic patients was significantly lower (by 54%; P lt 0.05) than in normal subjects. With GLP-1 (7-36-amide) **type-2** diabetic patients reached 71% of the increments in C-peptide of normal subjects (difference not significant). **Glucagon** was lowered during hyperglycemic clamps in normal subjects, but not in **type-2** diabetic patients, and further by GLP-1 (7-36-amide) in both groups (P lt 0.05), but not by GIP. In conclusion, in mild **type-2 diabetes**, GLP-1 (7-36-amide), in contrast go GIP, retains much of its insulinotropic activity. It also lowers **glucagon** concentrations.
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Set	Items	Description
S1	5715	GLUCAGON AND (TYPE(W)2 OR TYPE(W)II OR NIDDM) AND DIABETES
S2	1360	S1 AND PY<1994
S3	765	RD S2 (unique items)
S4	293	S3 AND (TREAT? OR ADMINISTER? OR (IN(W)VIVO))

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5/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008770124 BIOSIS NO.: 199395072390
Cellular and humoural autoimmunity markers in **Type 2** (non-insulin-dependent) diabetic patients with secondary drug failure
AUTHOR: Zavala A V (Reprint); Fabiano De Bruno L E; Cardoso A I; Mota A H; Capucchio M; Poskus E; Fainboim L; Basabe J C
AUTHOR ADDRESS: Catedra de Nutricion, Hospital de Clinicas, Av. Cordoba 2351, Buenos Aires, Argentina**Argentina
JOURNAL: Diabetologia 35 (12): p1159-1164 **1992**
ISSN: 0012-186X
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In some Cases patients with **Type 2** (non-insulin-dependent) **diabetes** mellitus fail to respond to **treatment** with oral hypoglycaemic agents. These patients may respond in the same way as Type 1 (insulin-dependent) diabetic patients. Cellular immune aggression (defined as the capacity of peripheral mononuclear cells to inhibit stimulated insulin secretion by dispersed rat islet cells), insulin autoantibodies, C-peptide response and HLA antigens were determined in 31 **Type 2** diabetic patients with secondary failure to oral hypoglycaemic agents and in 22 control subjects. Nine (29.03%) of the 31 **Type 2** diabetic patients showed positive cellular immune aggression (2 SD below control group) and 22 (70.97%) presented no cellular immune aggression. There was a relationship between positive cellular immune aggression and each of the following parameters: age, body mass index and microangiopathy. No correlation was found between positive cellular immune aggression and glycaemia HbA-1, blood lipids or atherosclerosis. Patients with positive cellular immune aggression showed a significantly lowel **glucagon** -stimulated C-peptide response vs those with no cellular immune aggression. Within a sub-group of patients who had never been **treated** with insulin, insulin autoantibodies were present in four of six patients with positive cellular immune aggression. DR2 antigen was found with decreased frequency in patients whereas no DR3/DR4 heterozygotes were observed. Our data support the hypothesis that a group of **Type 2** diabetic patients with secondary failure to oral hypoglycaemic agents presented autoimmunity towards pancreatic Beta cells.

5/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008763462 BIOSIS NO.: 199395065728
Insulin-like growth factor-I improves glucose and lipid metabolism in **type 2 diabetes** mellitus
AUTHOR: Zenobi Peter D (Reprint); Jaeggi-Groisman Silvia E; Riesen Walter F ; Roder Michael E; Froesch E Rudolf
AUTHOR ADDRESS: Div. Endocrinol. and Metabolism, Dep. Intern. Med., University Hosp., 8091 Zurich, Switzerland**Switzerland
JOURNAL: Journal of Clinical Investigation 90 (6): p2234-2241 **1992**
ISSN: 0021-9738
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Hyperglycemia, hyperinsulinemia, and insulin resistance cause vascular disease in **type 2 diabetes** mellitus. Dietary **treatment** alone often fails and oral drugs or insulin enhance hyperinsulinemia. In previous studies, an intravenous bolus of recombinant human insulin-like growth factor-I (rhIGF-I) caused normoglycemia in insulin-resistant diabetics whereas rhIGF-I infusions lowered insulin and lipid levels in healthy humans, suggesting that rhIGF-I is effective in insulin-resistant states. Thus, eight **type 2** diabetics on a diet received on five **treatment** days subcutaneous rhIGF-I (2 times 120 mu-g/kg) after five control days. Fasting and postprandial glucose, insulin, C-peptide, proinsulin, **glucagon**, triglyceride, insulin-like growth factor-I and -II, and growth hormone levels were determined. RhIGF-I administration increased total IGF-I serum levels 5.3-fold above control. During the control

period mean (+-SD) fasting glucose, insulin, C-peptide, and total triglyceride levels were 11.0+-4.3 mmol/liter, 108+-50 pmol/liter, 793+-250 pmol/liter, and 3.1+-2.7 mmol/liter, respectively, and decreased during **treatment** to a nadir of 6.6+-2.5 mmol/liter, 47+-18 pmol/liter, 311+-165 pmol/liter, and 1.6+-0.8 mmol/liter (P lt 0.01), respectively. Postprandial areas under the glucose, insulin, and C-peptide curve decreased to 77+-13 (P lt 0.02), 52+-11, and 60+-9% (P lt 0.01) of control, respectively. RhIGF-I decreased the proinsulin/insulin ratio whereas **glucagon** levels remained unchanged. The magnitude of the effects of rhIGF-I correlated with the respective control levels. Since rhIGF-I appears to improve insulin sensitivity directly and/or indirectly, it may become an interesting tool in **type 2 diabetes** and other states associated with insulin resistance.

5/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008720384 BIOSIS NO.: 199395022650
Effect of cigarette smoking and of a transdermal nicotine delivery system on glucoregulation in **type 2 diabetes** mellitus
AUTHOR: Epifano L; Di Vincenzo A; Fanelli C; Porcellati F; Perriello G; De Feo P; Motolese M; Brunetti P; Bolli G B (Reprint)
AUTHOR ADDRESS: Istituto Med. Interna, Sci. Endocrine Metaboliche, Via E. Dal Pozzo, I-06126 Perugia, Italy**Italy
JOURNAL: European Journal of Clinical Pharmacology 43 (3): p257-263
1992
ISSN: 0031-6970
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The effect of nicotine absorbed transdermally from a patch (TNS) and from cigarette smoking on insulin secretion and action in **Type 2 diabetes** has been compared. Twelve **Type 2** diabetic smoking patients, aged 51 y, with **diabetes** for 9 y, **treated** either with diet and/or oral hypoglycaemic agents, were studied on three occasions, according to a double-blind, placebo-controlled, cross- over design. The subjects were investigated 12 h after their last cigarette or application of one patch of TNS 30 cm-2 or TNS placebo, or whilst smoking their usual cigarette. Insulin secretion was assessed by a **glucagon** (1 mg IV) stimulation test. On a second occasion, insulin action was assessed by a hyperglycaemic-hyperinsulinaemic clamp, the spontaneous hyperglycaemia of the fasting state (8.61 mmol cntdot l-1) being maintained during a 4 h insulin infusion (at 0.1 mU cntdot kg-1 cntdot min-1 for the intial 2 h, and 1 mU cntdot kg-1 cntdot min-1 during the last 2 h). TNS and the cigarette did not affect endogenous insulin secretion as compared to placebo. During the initial 2 h of the clamp study, plasma insulin increased from 88 to 155 pmol cntdot l-1, hepatic glucose production (3-3H-glucose) was less suppressed after TNS (4.31 mu-mol cntdot kg-1 cntdot min-1) than after placebo (2.5 mu-mol cntdot kg-1 cntdot min-1), but was more suppressed than after cigarette smoking (5.61 mu-mol cntdot kg-1 cntdot min-1). In the last 2 h of the clamp (plasma insulin 646 pmol cntdot l-1), glucose utilization was less stimulated after TNS (36.1 mu-mol cntdot kg-1 cntdot min-1) vs placebo (39.8 mu-mol cntdot kg-1-1 cntdot min-1), but more than after cigarette smoking (33.6 mu-mol cntdot kg-1 cntdot min-1), primarily because of a decrease in glucose storage. Free fatty acid and lipid oxidation were significantly less suppressed by hyperinsulinaemia after TNS and cigarette smoking vs placebo. Nicotine impairs insulin action on the liver, adipose tissue and muscle and mah

contribute to hyperglycaemia in **Type 2 diabetes**. TNS diminishes the action of insulin to a lesser extent than cigarette smoking. Thus, TNS may respresent a "metabolically" safe measure to help patients with **Type 2 diabetes** to quit smoking.

5/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008422399 BIOSIS NO.: 199294124240
LONG-TERM **TREATMENT** WITH SIMVASTATIN IN HYPERCHOLESTEROLEMIC NON-INSULIN-DEPENDENT DIABETIC PATIENTS
AUTHOR: ZAMBON S (Reprint); LAPOLLA A; SARTORE G; GHERARDINGHER C; CORTELLA A; MANZATO E; CREPALDI G; FEDELE D
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JOURNAL: Current Therapeutic Research 52 (2): p221-229 **1992**
ISSN: 0011-393X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) show a high risk for coronary heart disease and frequently exhibit lipid and lipoprotein abnormalities. The efficacy and safety of simvastatin, a hydroxymethylglutaryl coenzyme A reductase inhibitor, were evaluated in 13 **NIDDM** patients (10 women and 3 men, aged 54 to 70 years, 11 on diet and 2 on oral hypoglycemic agents) with high plasma cholesterol levels (297 .+-. 27 mg/dl, mean .+-. SD) and normal triglyceride levels (181 .+-. 62 mg/dl). The patients received placebo for 6 weeks and simvastatin (up to 23 .+-. 10 mg/day) over 24 weeks. Nine patients continued the simvastatin **treatment** for 48 weeks with 13 .+-. 5 mg/day. Cholesterol and triglyceride levels in plasma and in lipoprotein fractions, isolated by preparative ultracentrifugation at density = 1.006 gm/ml, were measured before and after placebo, and after 6, 12, 18, 24, and 48 weeks of simvastatin **treatment**. Apoprotein (apo) AI and B determinations were also performed in plasma. Body mass index, fasting plasma glucose, C peptide before and after **glucagon**, and HbA1c did not change during the study period. Simvastatin reduced plasma cholesterol (31% after 24 weeks and 22% after 48 weeks), low-density lipoprotein cholesterol (37% after 24 weeks and 26% after 48 weeks), and apo B levels (39% after 24 weeks and 27% after 48 weeks). Very-low-density lipoprotein, high-density lipoprotein, and apo AI levels were not affected by **treatment**. No side effects were reported. Simvastatin appears to be an effective and safe hypocholesterolemic drug in patients with **NIDDM**.

5/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008410231 BIOSIS NO.: 199294112072
THE BETA CELL FUNCTION IN **NIDDM** PATIENTS WITH SECONDARY FAILURE A THREE YEAR FOLLOW-UP OF COMBINED ORAL HYPOGLYCEMIC AND INSULIN THERAPY
AUTHOR: GRECO A V (Reprint); CAPUTO S; BERTOLI A; GHIRLANDA G
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JOURNAL: Hormone and Metabolic Research 24 (6): p280-283 **1992**
ISSN: 0018-5043
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Eleven **Type 2** (non-insulin-dependent) diabetic patients, islet cell autoantibodies negative, nonobese with secondary failure to oral hypoglycemic agents (OHA) [glyburide (7.5 mg/day) and phenformin (75 mg/day)] and HbA1c 10.2 .+-. 0.6% were studied. Insulin receptors on circulating monocytes, glucose utilization at supraphysiological insulin concentrations, and plasma C-peptide after i.v. **glucagon** were evaluated before and after 2 months of combined therapy with OHA and insulin (ultratard HM Novo). A significant improvement was demonstrated in HbA1c and glycemia after two months of **treatment**. Glucose MCR was increased after two months of **treatment** whilst basal C-peptide was decreased as well as receptor binding to monocytes. After three years of combined therapy, body weight, glycemia and HbA1c did not increase. After three years the C-peptide basal values were significantly increased with respect to values found after 2 months of therapy. These results demonstrate that insulin **treatment** may restore insulin sensitivity in **NIDDM** patients resistant to OHA **treatment** and that after three years there is no exhaustion of B-cell function.

5/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008397789 BIOSIS NO.: 199294099630
NICARDIPINE DOES NOT CAUSE DETERIORATION OF GLUCOSE HOMEOSTASIS IN MAN A PLACEBO CONTROLLED STUDY IN ELDERLY HYPERTENSIVES WITH AND WITHOUT **DIABETES** MELLITUS
AUTHOR: GIUGLIANO D (Reprint); SACCOMANNO F; PAOLISO G; CERIELLO A; TORELLA R; VARRICCHIO M; D'ONOFRIO F
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JOURNAL: European Journal of Clinical Pharmacology 43 (1): p39-45
1992
ISSN: 0031-6970
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of calcium antagonist nicardipine on insulin secretion and glucose homeostasis was investigated in elderly hypertensives with and without **diabetes** mellitus; 15 patients with essential hypertension for at least 10 years and normal glucose tolerance according to standard criteria (Group I) and 15 elderly hypertensive patients affected by **Type 2 diabetes** mellitus and on **treatment** with diet or oral drugs (Group 2). In the basal state, all patients were submitted to an oral glucose tolerance test (OGTT, 75 g) and an iv arginine test (30 g), on two different days and in random order. The same tests were repeated after one month of **treatment** with nicardipine 60 mg/day, in three spaced doses, the last being given 1 h before the post-**treatment** test. Nicardipine did not change overall glucose homeostasis, as assessed by haemoglobin Alc and fructosamine, nor did it significantly affect the plasma insulin response either to glucose or arginine in Groups 1 and 2. Only the **glucagon** response to arginine was significantly reduced in diabetic hypertensives. Small, non-significant variations in the metabolic and hormonal parameters were seen in additional two groups of patients (Groups 3 and 4), matched with Groups 1 and 2 for age, sex and diseases, who took capsules containing placebo. Thus, nicardipine did not produce any significant overall alteration in glucose homeostasis when given to

elderly diabetic or nondiabetic hypertensive subjects.

5/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008392947 BIOSIS NO.: 199294094788
SOME MOLECULAR MECHANISMS INVOLVED IN THE PATHOGENESIS OF NON-INSULIN DEPENDENT **DIABETES** MELLITUS AND THEIR POTENTIAL THERAPEUTIC IMPORTANCE
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JOURNAL: Schweizerische Medizinische Wochenschrift 122 (30): p1109-1116 **1992**
ISSN: 0036-7672
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: FRENCH

ABSTRACT: The pancreatic beta cell presents functional abnormalities in the early stages of development of non-insulin dependent **diabetes** mellitus (**NIDDM**). The disappearance of the first phase of insulin secretion induced by a glucose load is a early marker of **NIDDM**. This abnormality could be secondary to the low expression of the pancreatic glucose transporter GLUT2. Together with the glucokinase enzyme, GLUT2 is responsible for proper beta cell sensing of the extracellular glucose levels. In **NIDDM**, the GLUT2 mRNA levels are low, a fact which suggests a transcriptional defect of the GLUT2 gene. The first phase of glucose-induced insulin secretion by the beta pancreatic cell can be partly restored by the administration of a peptide discovered by a molecular approach, the **glucagon**-like peptide 1 (GLP-1). The gene encoding for the **glucagon** is expressed in a cell-specific manner in the A cells of the pancreatic islet and the L cells of the intestinal tract. The maturation process of the propeptide encoded by the **glucagon** gene is different in the two cells: the **glucagon** is the main hormone produced by the A cells whereas the **glucagon**-like peptide 1 (GLP-1) is the major peptide synthesized by the L cells of the intestine. GLP-1 is an incretin hormone and is at present the most potent insulinotropic peptide. The first results of the administration of GLP-1 to normal volunteers and diabetic patients are promising and may be a new therapeutic approach to **treating** diabetic patients.

5/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008378409 BIOSIS NO.: 199294080250
ENCAINIDE-INDUCED **DIABETES** ANALYSIS OF ISLET CELL FUNCTION
AUTHOR: WINTER W E (Reprint); FUNAHASHI M; KOONS J
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JOURNAL: Research Communications in Chemical Pathology and Pharmacology 76 (3): p259-268 **1992**
ISSN: 0034-5164
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Objective: The purpose of this study was to gain insight into the mechanisms responsible for encainide-induced **diabetes**. Specifically, we sought to determine if absolute insulinopenia was present or whether encainide-induced **diabetes** was metabolically more like **type II** than type I **diabetes**. Research Design and Methods: Islet function was assessed in a 65 year old white male with encainide-induced **diabetes**. After 6 months of encainide **treatment** and 2 months duration of **diabetes**, C-peptide, **glucagon**, and glucose levels were measured at baseline and at 30 minute intervals for 120 minutes following an oral mixed meal. These measurements allowed assessment of islet beta and alpha cell function in comparison to control data from our laboratory. Results: In this patient with encainide-induced **diabetes**, basal and peak C-peptide concentrations were similar to controls although peak C-peptide occurred substantially later than in controls. At peak glucose, the patient's C-peptide/glucose ratio was low indicating relative (but not absolute) insulinopenia. At baseline, **glucagon** was relatively depressed. Following Sustacal, there was an increase in **glucagon** of 100% over baseline compared to a mean **glucagon** rise in controls by only 8%. There was no serological evidence for autoimmune **diabetes** as islet cell autoantbodies were absent. Conclusions: Similar to other forms of **diabetes**, encainide-induced **diabetes** is a bihormonal disorder. The metabolic pattern was more like **type II** than type I **diabetes** with C-peptide secretion in the normal range, yet persistent hyperglycemia that suggests relative insulinopenia and concurrent insulin resistance.

5/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008370303 BIOSIS NO.: 199294072144
GLUCAGON-STIMULATED INSULIN SECRETION IN PATIENTS WITH **TYPE 2 DIABETES** MELLITUS SUPPORT FOR THE CONCEPT OF GLUCOSE TOXICITY
AUTHOR: WOLFFENBUTTEL B H R (Reprint); MENHEERE P P C A; NIJST L; RONDAS-COLBERS G J W M; SELS J P J E; NIEUWENHUIJZEN KRUSEMAN A C
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JOURNAL: Netherlands Journal of Medicine International Edition 40 (5-6): p 277-282 **1992**
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Parameters of blood glucose control and insulin secretion were evaluated in 114 patients with **type 2 diabetes** mellitus, who were no longer controlled satisfactory by maximal doses of oral hypoglycaemic agents, and compared with those obtained in 11 healthy control subjects, 32 patients with recently-diagnosed **type 2 diabetes**, and 16 tablet-**treated** and 36 insulin-**treated** patients. Newly-diagnosed patients were slightly younger (60 .+-. 13 yr) and had a slightly higher body mass index (29.4 .+-. 6.5 kg/m2). Known duration of **diabetes** was 9 yr (range 1-37) in secondary failure, and 11 yr (range 1-31) in insulin-**treated** patients. Fasting blood glucose was the highest (13.8 .+-. 2.8 mmol/l) in secondary failure and newly-diagnosed patients (12.6 .+-. 3.8 nmol/l) compared to tablet-**treated** (8.7 .+-. 3.3 mmol/l) and insulin-**treated** patients (9.6 .+-. 3.2 mmol/l, $p < 0.05$). HbA1c levels were comparably elevated. In insulin-**treated** patients, fasting plasma C-peptide levels were lower relative to the mutually comparable levels in the other 3 diabetic

groups. Fasting plasma insulin levels did not differ between the 4 diabetic groups. C-peptide release after **glucagon** (C-peptide AUC) was comparable in all 4 diabetic groups, although in tablet-**treated** patients the ratio C-peptide AUC/fasting blood glucose was higher ($p < 0.05$). We conclude that the clinical usefulness of determining residual insulin secretion in **type 2** diabetic patients is limited, and that the similar reduction of insulin secretion in severely hyperglycaemic newly-diagnosed and secondary failure **type 2** diabetic patients supports the concept of "glucose toxicity".

5/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008370273 BIOSIS NO.: 199294072114
THE DAWN PHENOMENON AND **DIABETES** CONTROL IN **TREATED NIDDM** AND IDDM PATIENTS
AUTHOR: ATIEA J A (Reprint); LUZIO S; OWENS D R
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JOURNAL: Diabetes Research and Clinical Practice 16 (3): p183-190
1992
ISSN: 0168-8227
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of glycaemic control on the early morning plasma glucose rise, 'the dawn phenomenon', was assessed in two matching diabetic patient groups each comprising five **NIDDM** and two IDDM patients per group, who were otherwise considered to be in poor (HbA1 = 11.2 .+-. 0.6%) or good (HbA1 = 7.6 .+-. 0.2%) glycaemic control. Hourly plasma concentrations of glucose, insulin, **glucagon**, cortisol, and growth hormone were measured between 03.00 and 09.00 h. In all the poorly controlled diabetic patients the mean rise in plasma glucose between 06.00-08.00 and 03.00 h was .gtoreq. 1.0 mmol/l. In contrast, the plasma glucose increment was < 1.0 mmol/l in the well controlled diabetics. The overnight mean insulin levels in the poor and well controlled patient groups were 19.3 .+-. 0.5 and 25.0 .+-. 0.6 mU/l ($P < 0.001$) respectively. **Glucagon**, cortisol, and growth hormone levels in the early morning showed no significant differences between the two groups. The decline in plasma insulin from 03.00 to 08.00 h and mean cortisol level 03.00 and 06.00 h were both significantly correlated with the increase in plasma glucose between 03.00 and 08.00 h. We concluded that an increase of 1.0 mmol/l or more in plasma glucose during the early morning is of clinical importance.

5/7/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008352587 BIOSIS NO.: 199294054428
THE EFFECT OF VARIOUS BLOOD GLUCOSE LEVELS ON POST-**GLUCAGON** C-PEPTIDE SECRETION IN **TYPE 2** NON-INSULIN-DEPENDENT **DIABETES**
AUTHOR: NOSARI I (Reprint); LEPORE G; MAGLIO M L; CORTINOVIS F; PAGANI G
AUTHOR ADDRESS: ROTONDA DEI MILLE, 3-24100 BERGAMO, ITALY**ITALY
JOURNAL: Journal of Endocrinological Investigation 15 (2): p143-146
1992
ISSN: 0391-4097
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We investigated how different plasma glucose concentrations could significantly modify the C-peptide response to **glucagon**. Twenty poorly-controlled (HbA1c 10.2 .+-. 1.5%) non insulin-dependent (**NIDDM**) subjects (body mass index 27 .+-. 1.8), 2 **treated** with diet alone and 18 with oral hypoglycemic agents were studied. The first day **glucagon** (1 mg iv) was injected, patients being fasting and untreated. Mean plasma glucose levels were 11.4 .+-. 1.2 mM. On a second non consecutive day, after an overnight fast, the same patients were connected to a closed-loop insulin infusion system (Betalike, Genoa), their blood glucose concentrations were stabilized within a normoglycemic range (5-5.5 mM) for 2 h and insulin infusion was stopped. The **glucagon** test was repeated 30 min later. Blood samples were taken 0, 6, 10, 20 min after **glucagon** injection. In the second test basal, and 6, 10 and 20 min post-**glucagon** glucose levels were significantly lower ($p < 0.001$); similarly C-peptide concentrations were significantly reduced both in basal conditions (0.55 .+-. 0.04 vs 0.37 .+-. 0.04 mM; $p < 0.001$) and 6 (0.92 .+-. 0.06 vs 0.6 .+-. 0.06; $p < 0.001$), 10 (0.79 .+-. 0.06 vs 0.56 .+-. 0.06; $p < 0.001$) and 20 min (0.64 .+-. 0.05 vs 0.44 .+-. 0.04; $p < 0.001$) after stimulation. The C-peptide secretion area showed the same trend (49.5 .+-. 4.8 vs 32.1 .+-. 5.8; $p < 0.001$). In conclusion, our data confirms that blood glucose levels modulate the pancreatic insulin secretion; glycemic normalization significantly reduced both basal and post-**glucagon** C-peptide release.

5/7/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008325245 BIOSIS NO.: 199294027086
ANTIDIABETOGENIC EFFECT OF **GLUCAGON**-LIKE PEPTIDE-1 7-36-AMIDE IN NORMAL SUBJECTS AND PATIENTS WITH **DIABETES** MELLITUS
AUTHOR: GUTNIAK M (Reprint); ORSKOV C; HOLST J J; AHREN B; EFENDIC S
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JOURNAL: New England Journal of Medicine 326 (20): p1316-1322 **1992**
ISSN: 0028-4793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Background: **Glucagon**-like peptide-1 (7-36) amide (**glucagon**-like insulinotropic peptide, or GLIP) is a gastrointestinal peptide that potentiates the release of insulin in physiologic concentrations. Its effects in patients with **diabetes** mellitus are not known. Methods: We compared the effect of an infusion of GLIP that raised plasma concentrations of GLIP twofold with the effect of an infusion of slaine, on the meal-related release of insulin, **glucagon**, and somatostatin in eight normal subjects, nine obese patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**), and eight patients with insulin-dependent **diabetes** mellitus (IDDM). The blood glucose concentrations in the patients with **diabetes** were controlled by a closed-loop insulin-infusion system (artificial pancreas) during the infusion of each agent, allowing measurement of the meal-related requirement for exogenous insulin. In the patients with IDDM, normoglycemic-clamp studies were performed during the infusions of GLIP and saline to determine the effect of GLIP on insulin sensitivity. Results: In the normal subjects, the infusion of GLIP

significantly lowered the meal-related increases in the blood glucose concentration ($P < 0.01$) and the plasma concentrations of insulin and **glucagon** ($P < 0.05$ for both comparisons). The insulinogenic index (the ratio of insulin to glucose) increased almost 10-fold, indicating that GLIP had an insulinotropic effect. In the patients with **NIDDM**, the infusion of GLIP reduced the mean (.+-. SE) calculated isoglycemic meal-related requirement for insulin from 17.4 .+-. 2.8 to 2.0 .+-. 0.5 U ($P < 0.001$), so that the integrated area under the curve for plasma free insulin was decreased ($P < 0.05$) in spite of the stimulation of insulin release. In the patients with IDDM, the GLIP infusion decreased the calculated isoglycemic meal-related insulin requirement from 9.4 .+-. 1.5 to 4.7 .+-. 1.4 U. The peptide decreased **glucagon** and somatostatin release in both groups of patients. In the normoglycemic-clamp studies in the patients with IDDM, the GLIP infusion significantly increased glucose fertilization (saline vs. GLIP, 7.2 .+-. 0.5 vs. 8.6 .+-. 0.4 mg per kilogram of body weight per minute; $P < 0.01$). Conclusion: GLIP has an antidiabetogenic effect, and it may therefore be useful in the **treatment** of patients with **NIDDM**.

5/7/13 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008237956 BIOSIS NO.: 199293080847
METABOLIC EFFECTS OF NEW ORAL HYPOGLYCEMIC AGENT CS-045 IN **NIDDM** SUBJECTS
AUTHOR: SUTER S L (Reprint); NOLAN J J; WALLACE P; GUMBINER B; OLEFSKY J M
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JOURNAL: Diabetes Care 15 (2): p193-203 **1992**
ISSN: 0149-5992
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Objective: To study the metabolic effects of a new oral antidiabetic agent, CS-045, in subjects with non-insulin-dependent **diabetes** mellitus (**NIDDM**). Research Design and Methods: Eleven **NIDDM** subjects (mean age 59 yr and body mass index 32.3) were **treated** with 400 mg/day CS-045 for 6-12 wk. Patients were hospitalized before and at the end of the drug-**treatment** period for metabolic studies, including oral glucose tolerance test (OGTT), meal tolerance test (MTT), euglycemic glucose-clamp studies, and lipid analyses. Results: Eight subjects showed a marked clinical response to the drug, whereas 3 were nonresponders. The data were analyzed both for the total group and for the responders. Fasting plasma glucose (FPG) fell from 12.5 .+-. 0.7 to 10.7 .+-. 1.0 mM in the total group but fell more dramatically from 12.7 .+-. 0.5 to 8.3 .+-. 0.6 mM in the responder group. The area under the OGTT glucose curve improved by 17% in the total group and by 29% in the responders. The area under the MTT glucose curve improved by 38 and 52%, respectively. MTT levels of insulin, free fatty acids, and **glucagon** were significantly lower after **treatment**. Glucose disposal rates during glucose-clamp studies were increased in all subjects after CS-045 **treatment**. Mean increases were 63% at 120 mU .cntdot. m-2 .cntdot. min-1 and 41% at 300 mU .cntdot. m-2 .cntdot. min-1. Basal hepatic glucose production fell by 17% in total group and by 28% in the responders. Conclusions: CS-045 improves insulin resistance, reduces insulinemia, lowers hepatic glucose production, and improves both fasting and postprandial glycemia in **NIDDM** subjects. CS-045 may represent a new therapeutic option for **NIDDM**.

5/7/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008215860 BIOSIS NO.: 199293058751
EMBRYOTOXIC EFFECTS OF **DIABETES** ON PRE-IMPLANTATION EMBRYOS
AUTHOR: ORNOY A (Reprint); ZUSMAN I
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JOURNAL: Israel Journal of Medical Sciences 27 (8-9): p487-492 **1991**
ISSN: 0021-2180
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We describe the effects of metabolic diabetic factors and sera from diabetic animals and humans on the development of early pre-implantation mouse embryos. Our studies demonstrated that 20 to 24% of control mouse blastocysts failed to develop successfully when grown for 72 h in RPMI medium supplemented with 10% fetal bovine serum. D-glucose in concentrations > 3 mg/ml, insulin at concentrations of 0.5 and 1.0 IU/ml, **glucagon** in concentrations of .gtoreq. 10 .mu.g/ml, .beta.-hydroxybutyrate in concentrations > 5 mg/ml, and acetoacetate at concentrations of .gtoreq. 10 .mu.g/ml were all embryotoxic, the number of underdeveloped blastocytes rising to over 50%. The combination of these factors in relatively low concentrations was highly embryotoxic, especially when accompanied by hyperglycemia. The addition, to a control medium, of serum from nondiabetic rats (in concentrations of 20%) or of nondiabetic human serum (in concentrations of 50%) did not significantly change the rate of blastocystic development. Serum from streptozotocin-diabetic rats, in the same concentrations, increased the number of undeveloped embryos to 53%. With human diabetic sera the highest embryotoxic effect was found in type I **diabetes** with and without ketoacidosis. In **type II diabetes**, embryotoxic effects, although lower, were observed among all types studied [untreated, **treated** with insulin or with DAONIL (Hoechst, Germany)]. A high correlation was found between the number of undeveloped embryos and the blood concentrations of metabolic diabetic factors: glucose (in type I **diabetes**), .beta.-hydroxybutyrate (in **type II diabetes** untreated or **treated** with Daonil), acetoacetate (in insulin-**treated type II diabetes**), and HbA1c (in both insulin-**treated** and in Daonil-**treated type II diabetes**). The possible role of diabetic metabolic factors in causing increased risk of spontaneous abortions and infertility among diabetic women is discussed.

5/7/15 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008189814 BIOSIS NO.: 199293032705
SERUM KETONE RESPONSE TO **GLUCAGON** AS A MARKER OF INSULIN DEPENDENCY IN DIABETICS
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JOURNAL: Diabetes Research and Clinical Practice 14 (2): p107-112 **1991**
ISSN: 0168-8227
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The serum ketone response to **glucagon** was measured in 10 patients with IDDM and 37 with **NIDDM**. In both groups, serum 3-hydroxybutyrate increased significantly after intravenous injection of 1 mg **glucagon**. The difference between the serum level of 3-hydroxybutyrate at 30 min and basal level [.DELTA.3-OHBA(30')] was 133 .+-. 25 .mu.mol/l in the patients with IDDM, 13 .+-. 8 .mu.mol/l in those with **NIDDM treated** by diet alone or with oral hypoglycemic agents and 23 .+-. 13 .mu.mol/l in those with **NIDDM treated** with insulin. The .DELTA.3-OHBA(30') was significantly greater in IDDM patients than in both groups of **NIDDM** patients ($P < 0.001$). The .DELTA.3-OHBA(30') was greater than 87 .mu.mol/l in eighty percent of IDDM patients, but smaller than 87 .mu.mol/l in both groups of **NIDDM** patients. The .DELTA.3-OHBA(30') was correlated with the difference between the plasma level of C-peptide at 6 min and basal level [.DELTA.CPR(6')] ($r = -0.540$, $P < 0.001$). The .DELTA.3-OHBA(30') was not correlated with fasting plasma levels of glucose, fructosamine or hemoglobin A1c. These observations show that measurement of the serum ketone response to **glucagon** is a useful marker of insulin dependency. In order to determine insulin dependency, the simultaneous measurement of concentrations of ketones and C-peptide is indicated during the **glucagon** stimulation test.

5/7/16 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0008189685 BIOSIS NO.: 199293032576
EFFECT OF AN ORAL ALPHA-2-ADRENERGIC BLOCKER MK-912 ON PANCREATIC ISLET FUNCTION IN NON-INSULIN-DEPENDENT **DIABETES** MELLITUS
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JOURNAL: Metabolism Clinical and Experimental 40 (11): p1160-1167
1991
ISSN: 0026-0495
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We used MK-912, a potent new selective .alpha.2-adrenergic receptor antagonist that is active orally, to study the effect of short-term, selective .alpha.2-blockade on fasting plasma glucose (FPG) and pancreatic islet function in non-insulin-dependent **diabetes** (**NIDDM**). Ten asymptomatic patients with **NIDDM** received either a single oral dose of MK-912 (2 mg) or placebo in a double-blind, cross-over study. B-cell function was measured by the acute insulin response (AIR) to glucose (1.66 mmol/kg intravenously [IV]) and by the AIR to arginine (5 g IV) during a hyperglycemic glucose clamp at a mean glucose level of 32.1 mmol/L to provide an estimation of maximal B-cell secretory capacity. A-cell function was estimated by the acute **glucagon** response (AGR) to arginine during the glucose clamp. Effective .alpha.2-adrenergic blockade was apparently achieved, as there were substantial increases of plasma norepinephrine (NE) ($P < .01$) and both systolic blood pressure (SBP) ($P < .01$) and diastolic blood pressure (DBP) ($P < .05$) after **treatment** with MK-912, but not after placebo. MK-912 caused a significant ($P < .05$) although modest decrease of FPG that was associated with a small increase of fasting plasma insulin ($P <$

0.01), C-peptide (P < .05), and **glucagon** (P < .01). FPG and hormone levels remained unchanged after placebo. MK-912 tended to increase the AIR (P = .06) and the C-peptide response (P = .07) to glucose compared with placebo. There was a small, but significant, overall **treatment** effect for both the AIR and AGR to arginine with MK-912 (both P < .05, ANOVA). These studies indicate that MK-912 causes (1) sympathetic activation consistent with effective .alpha.2-adrenergic blockade; (2) a small decrease of FPG and small increase of fasting plasma insulin; (3) a small improvement of B-cell function due to an increase in maximal B-cell secretory capacity; and (4) a small increase in basal and stimulated **glucagon**. These findings suggest that endogenous .alpha.2-adrenergic tone may contribue, although to a small extent, to the impaired B-cell function in **NIDDM**. If an .alpha.2-blocker becomes available that does not increase BP, studies would be warranted to evaluate its potential impact on glucose regulation in patients with **NIDDM**.

5/7/17 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007877314 BIOSIS NO.: 199192123085
URINARY C-PEPTIDE AS AN INDEX OF UNSTABLE GLYCEMIC CONTROL IN INSULIN-DEPENDENT **DIABETES** MELLITUS IDDM
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JOURNAL: Diabetes Research and Clinical Practice 13 (3): p181-188
1991
ISSN: 0168-8227
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: In order to investigate whether urinary C-peptide (UCP) excretion can be a useful index of insulin-dependent **diabetes** mellitus (IDDM) with unstable glycemic control, UCP was measured in nine IDDM patients with unstable glycemic control, nine IDDM patients with stable glycemic control, and 12 non-insulin-dependent diabetic (**NIDDM**) patients **treated** with insulin. The UCPs in overnight urine (U1) and fasting single void urine (U2) in IDDM patients with unstable glycemic control were significantly lower than those in IDDM patients with stable glycemic control (U1: 0.03 .+-. 0.03 vs 0.24 .+-. 0.20 nmol/mmol-Creatinine, U2: 0.02 .+-. 0.01 vs 0.20 .+-. 0.20 nmol/mmol-Cr, mean .+-. SD, both P < 0.01). The UCPs in U1 and U2 in both groups of IDDM were significantly lower than those in **NIDDM** (U1: 0.97 .+-. 0.52, U2: 0.73 .+-. 0.41 nmol/mmol-Cr, both P < 0.01). The UCPs in U1 and U2 significantly correlated with incremental C-peptide response to intravenous **glucagon** injection and with glycemic stability assessed by the standard deviation of 10 previous fasting plasma glucose levels. These results suggest that UCP reflects their residual insulin secretory capacity and that UCP can be a useful index which distinguishes patients with unstable IDDM from those with stable **diabetes** mellitus.

5/7/18 (Item 18 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007817473 BIOSIS NO.: 199192063244

FIVE-YEAR FOLLOW-UP OF ISLET CELL ANTIBODIES IN **TYPE 2** NON-INSULIN-DEPENDENT **DIABETES** MELLITUS
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JOURNAL: Diabetologia 34 (6): p402-408 **1991**
ISSN: 0012-186X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The aim was to study the frequency and appearance of cytoplasmic islet cell antibodies in relation to impairment of insulin secretory capacity and some clinical characteristics in a representative group of middle-aged (45-64 years) patients with **Type 2** (non-insulin-dependent) **diabetes** mellitus (70 male, 63 female) at the time of diagnosis and at five-year follow-up. Non-diabetic control subjects (62 male, 82 female) were similarly examined at five-year intervals. At the baseline five out of 133 (3.8%) diabetic patients were positive for conventional and four (3.0%) for complement-fixing islet cell antibodies. Ten patients had become positive by the second screening for conventional antibodies and six for complement-fixing antibodies, but none showed negative conversion. Two non-diabetic subjects (1.5%) became antibody positive during the follow-up. Insulin **treatment** was started during the follow-up for four out of 15 (27%) conventional antibody positive and for one out of 121 (0.8%) antibody negative diabetic patients (up = 0.001). The sensitivity of the positive conventional and complement-fixing antibody for identifying patients who developed an impairment of insulin secretory capacity (post-**glucagon** C-peptide .ltoreq. 0.60 nmol/l at 5-year) was 75%. The respective specificity was 90% and the positive predictive values were highest in the case of high positivity (50%). The negative predictive value of antibody positivity was close to 100%. In conclusion, islet cell antibody positivity in patients classified as **Type 2** was persistent during the follow-up and predicted the future development of insulin deficiency especially in those patients with high or increasing antibody titres.

5/7/19 (Item 19 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007784627 BIOSIS NO.: 199192030398
AMYLIN-INDUCED **IN-VIVO** INSULIN RESISTANCE IN CONSCIOUS RATS THE LIVER IS MORE SENSITIVE TO AMYLIN THAN PERIPHERAL TISSUES
AUTHOR: KOOPMANS S J (Reprint); VAN MANSFELD A D M; JANSZ H S; KRANS H M J; RADDER J K; FROLICH M; DE BOER S F; KREUTTER D K; ANDREWS G C; MAASSEN J A
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JOURNAL: Diabetologia 34 (4): p218-224 **1991**
ISSN: 0012-186X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Amylin is a polypeptide of 37 amino acids, predominantly synthesized in pancreatic Beta cells. The peptide was suggested to be dysregulated in **Type 2** (non-insulin-dependent) **diabetes** mellitus and it antagonized certain actions of insulin in vitro in rat muscle. This led to speculation that amylin is involved in the

pathogenesis of **Type 2 diabetes**. We have examined the **in vivo** effects of rat amylin, amidated at the carboxy-terminus, on insulin-mediated carbohydrate metabolism in conscious rats, using the hyperinsulinaemic (.+-. 1 nmol/l) euglycaemic (6 mmol/l) clamp technique combined with [3-3H]-glucose infusion. Basal plasma amylin levels were .ltoreq. 75 pmol/l. Applied amylin levels of 220 .+-. 75 pmol/l (infusion rate of 12.5 pmol/min) antagonized only the insulin action on liver, resulting in a 100% increase of hepatic glucose output. Amylin levels of 4750 .+-. 750 pmol/l (infusion rate of 125 pmol/min) induced a 250% increase of insulin-inhibited hepatic glucose output and, in addition, a 30% decrease of insulin-stimulated peripheral glucose uptake. Amylin did not affect: the metabolic clearance rate of insulin, the levels of plasma **glucagon**, epinephrine, norepinephrine, and corticosterone, in vitro insulin binding and insulin-stimulated receptor autophosphorylation. This suggests that amylin antagonizes insulin action via binding to a yet unknown receptor. In conclusion: amylin causes **in vivo** insulin resistance and the liver seems the predominant organ regulated by this hormone. The **in vivo** effects of amylin mimic the pathophysiological abnormalities of insulin action in **Type 2 diabetes**.

5/7/20 (Item 20 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007711647 BIOSIS NO.: 199191094538
METABOLIC EFFECTS AND CLINICAL VALUE OF BEET FIBER **TREATMENT** IN **NIDDM** PATIENTS
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JOURNAL: Diabetes Research and Clinical Practice 11 (2): p65-72 **1991**
ISSN: 0168-8227
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: In the present study a randomized cross-over design was used to determine the clinical usefulness of adding 16 g of beet fiber to the ordinary diet of non-insulin dependent diabetic (**NIDDM**) out-patients. In addition, fiber effects on the gastrointestinal hormone responses to a standardized test meal were evaluated. The study included five patients **treated** with diet alone and eight patients **treated** with diet and sulphonylurea (SU). Beet fibers supplementation resulted in a 10% reduction ($P < 0.01$) of serum cholesterol in SU-**treated** patients. No differences were found for fasting blood glucose, glycated hemoglobin, serum triglycerides or body weight. In the diet-**treated** patients, fasting plasma somatostatin was elevated during the fiber period. However, postprandial responses of insulin, C-peptide, **glucagon**, gastric inhibitory peptide and somatostatin were not influenced by an increased fiber intake in any group. All patients experienced mild gastrointestinal discomfort during the fiber period. In view of the limited metabolic benefit of beet fiber **treatment** we conclude that there is little use for this type of dietary fiber in the routine **treatment** of patients with **NIDDM**
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5/7/21 (Item 21 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007666241 BIOSIS NO.: 199191049132
DIURNAL VARIATION OF BLOOD KETONE BODIES IN INSULIN-DEPENDENT **DIABETES** MELLITUS AND NON-INSULIN-DEPENDENT **DIABETES** MELLITUS PATIENTS THE RELATIONSHIP TO SERUM C PEPTIDE IMMUNOREACTIVITY AND FREE INSULIN
AUTHOR: UBUKATA E (Reprint)
AUTHOR ADDRESS: THIRD DEP INTERN MED, TEIKYO UNIV SCH MED, ICHIHARA, CHIBA 299-01, JAPAN**JAPAN
JOURNAL: Annals of Nutrition and Metabolism 34 (6): p333-342 **1990**
ISSN: 0250-6807
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We examined whether the rise in ketone body concentration around midnight and in the early morning was due to the lack of free insulin (IRI) or excess of insulin counterregulatory hormones such as human growth hormone (hGH), cortisol and **glucagon** in noninsulin-dependent **diabetes** mellitus (**NIDDM**) and insulin-dependent **diabetes** mellitus (IDDM) patients and whether the monitoring of blood ketone body concentration was clinically used as an index of metabolic control for deciding to increase or decrease the insulin dose in the **treatment** of **diabetes** mellitus. Serum levels of 3-hydroxybutyrate (3-OHBA), acetoacetate (AcAc) and 3-OHBA/AcAc ratio before breakfast were significantly increased in insulin-**treated** **NIDDM** patients with well-controlled fasting plasma glucose levels and IDDM patients compared to those in normal subjects. Mirror image diurnal changes were found between serum concentrations of 3-OHBA and serum C-peptide or free IRI in normal subjects and **NIDDM** patients **treated** with diet alone or sulfonylurea during the 24-hour daily profiles. However, there were no correlations between 3-OHBA and free IRI in the **NIDDM** patients **treated** with insulin and IDDM patients who had a much larger increase in the mean concentration of serum 3-OHBA at 6 a.m. caused by a low concentration of free IRI. Counterregulatory hormones were not increased in IDDM patients compared to normal subjects in the early morning. Cortisol/free IRI and hGH/free IRI molar ratios were significantly increased in **NIDDM** and IDDM patients compared to normal subjects in the early morning, but **glucagon**/free IRI molar ratio was not changed between IDDM and normal subjects. In conclusion, the early morning rising of ketone body concentration in insulin-**treated** diabetic patients, particularly IDDM patients, is due to the absolute lack of free IRI and/or the relative lack of free IRI to the levels of hGH or cortisol, and the monitoring of 3-OHBA is clinically useful as a more sensitivity index of metabolic control.

5/7/22 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007636988 BIOSIS NO.: 199191019879
COMBINED THERAPY WITH GLIBENCLAMIDE AND ULTRALENTE INSULIN IN LEAN PATIENTS WITH **NIDDM** WITH SECONDARY FAILURE OF SULFONYLUREAS FOLLOW-UP AT TWO YEARS
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JOURNAL: Diabete and Metabolisme 16 (4): p323-327 **1990**
ISSN: 0338-1684
DOCUMENT TYPE: Article
RECORD TYPE: Abstract

LANGUAGE: ENGLISH

ABSTRACT: Nine lean diabetic patients with secondary failure of oral hypoglycemic agents and with a poor residual insulin release under **treatment** with glibenclamide (15 mg/day) entered a cross-over study, in which ultralente insulin was **administered** alone or in combination with glibenclamide (15 mg/day). Combined therapy was accompanied by increased serum free-insulin levels and was more effective than glibenclamide alone on daily blood glucose profile, on glycosylated haemoglobin (HbA1C) and on Beta-OH butyrate; in 6 patients a near normalization of blood glucose control (daily blood glucose levels < 180 mg/dl) occurred. C peptide release, evaluated as daily profile and as response to i.v. **glucagon**, did not significantly change. When patients received insulin alone, daily blood glucose profile and HbA1C worsened, and serum free-insulin levels and C peptide release decreased, while Beta-OH butyrate levels remained low. These data indicate that combined therapy is effective since it maintains insulin release and enhances free insulin levels in insulinopenic patients. Four responders continued combined therapy for 2 years: the **treatment** was still effective and was accompanied by an increased C peptide release, probably due to persistent euglycemia.

5/7/23 (Item 23 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007583826 BIOSIS NO.: 199141096452
LONG TERM COMBINED INSULIN SULFONYLUREA **TREATMENT** IN **TYPE II DIABETES** EFFECTS ON ENDOGENOUS INSULIN SECRETION
AUTHOR: SEGERS O (Reprint); BRASSEUR L; DE SAEDELEER C; KEYMEULEN B; SOMERS G
AUTHOR ADDRESS: VRIJE UNIV BRUSSELS, BRUSSELS, BELGIUM**BELGIUM
JOURNAL: European Journal of Clinical Investigation 21 (2 PART 2): p19 **1991**
CONFERENCE/MEETING: 25TH MEETING OF THE EUROPEAN SOCIETY FOR CLINICAL INVESTIGATION, PISA, ITALY, APRIL 3-6, 1991. EUR J CLIN INVEST.
ISSN: 0014-2972
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

5/7/24 (Item 24 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007342005 BIOSIS NO.: 199090126484
EFFECTS OF GLYBURIDE ON **IN-VIVO** INSULIN-MEDIATED GLUCOSE DISPOSAL
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AUTHOR ADDRESS: JOSLIN DIABETES CENTER, ONE JOSLIN PLACE, BOSTON, MASS 02215, USA**USA
JOURNAL: American Journal of Medicine 89 (2 PART A): p44S-50S **1990**
ISSN: 0002-9343
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The purpose of this study was to examine the effects of glyburide on peripheral (muscle) and hapatic insulin sensitivity in patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) and

insulin-dependent **diabetes** mellitus (IDDM) as well as in healthy control subjects. In protocol 1, 10 patients with **NIDDM** and seven young healthy control subjects were studied. Changes in insulin sensitivity (40 mU/m2 .cntdot. min euglycemic insulin clamp), hepatic glucose production (3-[3H]glucose turnover), and insulin secretion (+125 mg/dL hyperglycemic clamp) were measured before and after 3 months (in patients with **NIDDM**) and 6 weeks (in young control subjects) of glyburide therapy. In protocol 2, five patients with IDDM and eight patients with insulin-**treated NIDDM** were evaluated before and after two months of glyburide therapy (20 mg per day). Changes in daily insulin requirements, 24-hour plasma glucose profiles, glycohemoglobin, **glucagon**-stimulated C-peptide secretion, insulin sensitivity, and hepatic glucose production were measured. In protocol 1, glyburide significantly improved insulin sensitivity ($p < 0.01$) and insulin secretion ($p < 0.01$) in the **NIDDM** patients. The elevated rates of hepatic glucose production (2.4 .+-. 0.3 mg/kg .cntdot. min) were reduced after glyburide therapy (1.7 .+-. 0.2 mg/kg .cntdot. min; $p < 0.01$) and were highly correlated with an improvement in fasted plasma glucose levels ($r = 0.92$; $p < 0.001$). Insulin sensitivity also improved in the young healthy control subjects after glyburide therapy (6.5 .+-. 0.5 to 7.6 .+-. 0.7 mg/kg .cntdot. min; $p < 0.05$). In protocol 2, glyburide **treatment** produced no change in daily insulin requirement (54 .+-. 8 versus 53 .+-. 7 units per day), mean 24-hour glucose levels (177 .+-. 20 versus 174 .+-. 29 mg/dL), glycohemoglobin (10.1 .+-. 1.0 percent versus 9.5 .+-. 7 percent), C-peptide secretion, insulin sensitivity, or basal hepatic glucose production (p values not significant) in the IDDM patients. In contrast, the insulin-**treated NIDDM** patients had significant reductions in mean daily insulin requirement (72 .+-. 6 versus 58 .+-. 9 units per day; $p = 0.05$), mean 24-hour plasma glucose levels (153 .+-. 10 to 131 .+-. 5 mg/dL; $p < 0.05$), and glycohemoglobin levels (10.3 .+-. 0.7 percent to 8.0 .+-. 0.4 percent; $p < 0.05$) and an improvement in C-peptide secretion (0.24 .+-. 0.07 to 0.44 .+-. 0.09 pmol/mL; $p = 0.08$). Stimulated C-peptide levels were highly correlated with a reduction in insulin dose observed during the 2-month **treatment** period ($r = 0.93$; $p < 0.001$). Insulin sensitivity improved slightly but not significantly after glyburide **treatment**. It is concluded that glyburide improves glycemic control by a combination of mechanisms, including: (1) enhancement of peripheral (muscle) insulin sensitivity; (2) reduction in basal hepatic glucose production; and (3) potentiation of glucose-stimulated insulin secretion. Because no benefit is observed in IDDM patients, it appears that some endogenous insulin secretory capacity is required for these effects to become evident.

5/7/25 (Item 25 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007253857 BIOSIS NO.: 199090038336
THE CLINICAL AND HORMONAL C PEPTIDE AND **GLUCAGON** PROFILE AND LIABILITY TO KETOACIDOSIS DURING NUTRITIONAL REHABILITATION IN ETHIOPIAN PATIENTS WITH MALNUTRITION-RELATED **DIABETES** MELLITUS
AUTHOR: ABDULKADIR J (Reprint); MENGESHA B; WELDE GEBRIEL Z; KEEN H; WORKU Y; GEBRE P; BEKELE A; URGA K; TADDESSE A-S
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JOURNAL: Diabetologia 33 (4): p222-227 **1990**
ISSN: 0012-186X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Cases of malnutrition-related **diabetes** mellitus conforming

to the description of the protein deficient pancreatic **diabetes** type in Ethiopian patients were compared with Type 1 (insulin-dependent) and **Type 2** (non-insulin-dependent) diabetic. Fourteen of 39 malnutrition-related **diabetes** mellitus patients had fat malabsorption compared with only two of ten Type 1 diabetic patients and one of nine control subjects. Xylose absorption was normal favouring a pancreatic cause for the malabsorption. Plasma C-peptide during oral glucose tolerance test was significantly lower than that in **Type 2** diabetic patients and normal control subjects ($p < 0.01$ to 0.001) and was also consistently but not significantly higher than in Type 1 diabetic patients. **Glucagon** secretion patterns were similar in malnutrition-related and Type 1 diabetic patients. Of 23 new malnutrition-related diabetic patients **treated** with glibenclamide after nutritional rehabilitation and insulin **treatment**, only three responded, 14 were unresponsive but remained ketosis free for over eight days while another six developed ketoacidosis or significant ketonuria within two to six days during the trial. Sixteen unselected Type 1 diabetic patients who discontinued their insulin therapy all developed frank ketoacidosis after a mean of 5.5 days. The similarity of the malnutrition-related and Type 1 **diabetes** mellitus in age of onset, insulin requirement for diabetic control and appearance of ketosis-proneness in some cases, together with the similarity of C-peptide and **glucagon** secretion patterns suggest that the protein deficient pancreatic **diabetes** variant of malnutrition-related **diabetes** mellitus may be Type 1 **diabetes** mellitus modified by the background of malnutrition rather than an aetiologically separate entity. Community based studies are required to ascertain frequency and types of **diabetes** mellitus in malnourished populations and the role of genetics and environment in their aetiology.

5/7/26 (Item 26 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007247312 BIOSIS NO.: 199090031791
THE RATIONALITY AND EFFECTIVENESS OF INSULIN THERAPY IN ELDERLY PATIENTS WITH **TYPE II DIABETES**
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JOURNAL: Diabetologia Croatica 18 (4): p163-170 **1989**
ISSN: 0351-0042
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The aim of the study was to ascertain the rationality and effectiveness of insulin therapy in the **treatment** of **type II diabetes** and to ascertain whether there are any indications which would enable us to find out in which poorly controlled **type II** diabetics receiving a maximum daily dose of oral drugs is there a real failure of oral therapy and in which causes of poor metabolic functioning are to be sought elsewhere. We analyzed the data of 188 **type II** diabetics who were hospitalized because of suspected drug failure. After a clinical trial it was established that 128 needed insulin (Group A), 28 insulin and oral antidiabetic drugs (Group C) and the remaining 34 could leave the hospital only on oral therapy (Group B). There were no significant difference ($p < 0.05$) between the groups as to the age of the patients, age duration of **diabetes**, BMI, C-peptide excreted in 24 hour urine, fasting serum

C-peptide and serum C-peptide after a **glucagon** simulation test. There were differences, however, in fasting glycemia and HbA1. Results at 1, 6 and 12 months after discharge (*: results at admission): Group A: glucemia: 12,1 .+-. 3.3*, 11.0 .+-. 3.2*, 10.6 .+-. 3.* mmol/l; HbA1: 11.3 .+-. 1.6*, 9.2 .+-. 1.4*, 9.1 .+-. 1.5* %; Group B: glycemia: 11.4 .+-. 4.0*, 12.5 .+-. 3.3, 11.9 .+-. 2.4 mmol/l; HbA; 9.4 .+-. 1.2*, 9.9 .+-. 2.1*. 11.3 .+-. 2.7*, 11.6 .+-. 3.0* mmol/l; HbA1: 10.2 .+-. 1.6(, 9.0 .+-. 1.8*, 8.7 .+-. 1.5* %. (*: statistically significant difference at $p < 0.05$). There were no statistical differences among the groups as far as glycemia and HbA1 in different time periods. We conclude that a significant and longterm improvement of metabolic control occur in patients who had been switched to insulin because of a secondary drug failure, while improvement was only temporary in the group of patients in which the causes of poor metabolic functioning were elsewhere and so these patients could continue **treatment** with hypoglycemic drugs. Because of a high overlapping of results obtained in the groups due to high variance, unfortunately it is not possible to classify patients into either group merely on the basis of observed parameters without a clinical trial.

5/7/27 (Item 27 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007123533 BIOSIS NO.: 199089041424
DRUG CONSUMPTION IN ELDERLY DIABETICS
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JOURNAL: Diabetes Research and Clinical Practice 7 (4): p293-298
1989
ISSN: 0168-8227
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The drug use in 228 persons with **diabetes** was studied and compared with that of sex- and age-matched non-diabetic controls-all of whom were found by the screening of a well-defined Danish population aged 60-74 years. Ninety per cent of the diabetics had non-insulin-dependent **diabetes** mellitus (**NIDDM**), as evaluated by a **glucagon** -C-peptide test. Information on daily use of prescribed and non-prescribed drugs was obtained by questionnaires and interviews. More than 80% of the diabetics used drugs daily, compared to 55% of control subjects ($P < 0.00001$). Among subjects using drugs diabetics, on average, used 70% more defined daily doses (DDD) than controls, even when antidiabetics were excluded. There was no difference in the number of drug users among subgroups of diabetics when divided according to antidiabetic **treatment** but tablet-**treated** diabetics, on average, used 20% fewer DDD than other diabetics. Cardiovascular drugs drugs were the most commonly used drugs. Diabetics in all antidiabetic **treatment** groups used significantly more cardiovascular drugs than non-diabetics. Diabetics **treated** with oral antidiabetics used fewer cardiovascular drugs than insulin- and diet-**treated** diabetics. The estimated cost of drug therapy was more than 2.5 times higher for diabetics than for the control group. Our results reflect the increased morbidity among elderly diabetics and emphasise, together with other aspects of costs of **diabetes** in the elderly, the need for allocating resources for the prevention of **NIDDM** instead of the **treatment** of its complications.

5/7/28 (Item 28 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007099870 BIOSIS NO.: 199089017761
LOW-DOSE BEDTIME NPH INSULIN IN **TREATMENT** OF SECONDARY FAILURE TO GLYBURIDE
AUTHOR: TRISCHITTA V (Reprint); ITALIA S; BORZI V; TRIBULATO A; MAZZARINO S ; SQUATRITO S; VIGNERI R
AUTHOR ADDRESS: CATEDRA ENDOCRINOL, OSPED GARIBALDI, PIAZZA SANTA MARIA DI GESU, 95123 CATANIA, ITALY**ITALY
JOURNAL: Diabetes Care 12 (8): p582-585 **1989**
ISSN: 0149-5992
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Secondary failure to oral hypoglycemic agents (OHAs) is a possible outcome for non-insulin-dependent **diabetes** mellitus (**NIDDM**) patients and poses a serious therapeutic problem. In this study, we evaluated the effect of adding a single bedtime low-dose NPH insulin injection to the previous ineffective sulfonylurea therapy in 23 **NIDDM** patients with true secondary failure to OHAs. This **treatment** schedule was conducted for 3 mo by 18 patients (78%) who completed the study. In these patients, the addition of NPH insulin (0.2 .+-. 0.01 IU/kg body wt) greatly decreased fasting and postprandial plasma glucose (P < .001) and glycosylated hemoglobin (P < .005). No weight gain was observed in any of the patients studied. Five patients dropped out: 2 patients (9%) due to insufficient compliance, 2 patients (9%) due to the multiple insulin injections required to achieve good metabolic control, and 1 patient (4%) due to recurrent hypoglycemic episodes. No correlation was observed between **glucagon**-stimulated C-peptide values and amelioration of metabolic control. In conclusion, most **NIDDM** patients with secondary failure to OHAs may be successfully **treated** with the addition of a single low-dose bedtime NPH insulin injection, and residual .beta.-cell function evaluation is not able to predict the effectiveness of the combined **treatment**.

5/7/29 (Item 29 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0007018815 BIOSIS NO.: 199039072204
THE PATHOPHYSIOLOGY OF **TYPE II** NONINSULIN-DEPENDENT **DIABETES** MELLITUS IMPLICATIONS FOR **TREATMENT**
BOOK TITLE: RIFKIN, H. AND D. PORTE, JR. (ED.). ELLENBERG AND RIFKIN'S **DIABETES** MELLITUS: THEORY AND PRACTICE, FOURTH EDITION. XVI+972P. ELSEVIER SCIENCE PUBLISHING CO., INC.: NEW YORK, NEW YORK, USA; AMSTERDAM, NETHERLANDS. ILLUS
AUTHOR: KAHN S E (Reprint); PORTE D JR
AUTHOR ADDRESS: DIV METAB ENDOCRINOL NUTR, DEP MED, UNIV WASH SCH MED, SEATTLE, WASH, USA**USA
p436-456 **1990**
ISBN: 0-444-01499-3
DOCUMENT TYPE: Book
RECORD TYPE: Citation
LANGUAGE: ENGLISH

5/7/30 (Item 30 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

0006762458 BIOSIS NO.: 198988077573
SECONDARY FAILURE WITH ORAL HYPOGLYCEMIC AGENTS IN NON-OBESE PATIENTS WITH NON-INSULIN-DEPENDENT **DIABETES** IS RELATED TO REDUCED INSULIN RELEASE
AUTHOR: PONTIROLI A E (Reprint); CALDERARA A; MAFFI P; BONISOLLI L; CARENINI A; PIATTI P M; MONTI L D; GALLUS G; POZZA G; ILLENI M T
AUTHOR ADDRESS: OSPEDALE S RAFFAELE, OLGETTINA 60-20132 MILANO, ITALY** ITALY
JOURNAL: Diabete and Metabolisme 15 (2): p79-84 **1989**
ISSN: 0338-1684
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The frequency of secondary failure to oral hypoglycaemic agents (OHA) in patients with non-insulin dependent **diabetes** (**NIDDM**) is still unknown, despite more than 30 years of use of OHA. The term secondary failure should be limited to patients who, despite maximal dosages of OHA and despite full compliance with diet and therapy, are no longer controlled and require insulin to obtain an acceptable glucose metabolism. We evaluated 248 out-patients, either on OHA, or on insulin because of poor metabolic control with OHA, in order to assess duration of **treatment** with OHA since diagnosis, by means of actuarial curves (Mantel-Cox test). Patients with low relative body weight (RBW .ltoreq. 100) experienced secondary failure earlier and more often than obese patients (RBW > 120) or overweight (RBW 101-120) patients. In 66 of the above out-patients, 33 OHA-**treated** and 33 insulin-**treated**, matched for age at onset adn duration of disease, islet-cell-antibodies (ICA) and C-peptide release at fasting, 6 min after i.v. **glucagon** and post prandially were evaluated. Only among lean and overweight patients, was C-peotode release significantly lower in insulin-**treated** than in OHA-**treated** patients; differences disappeared in obese patients. ICA were found in only 7 patients (10.6%). HLA phenotype was different from that of healthy blood donors for the loci HLA B5, B14, CW4, with no differences between OHA-**treated** and insulin-**treated** patients. These data indicate that secondary failure is more frequent in lean patients with **NIDDM**, and is related to reduce insulin release.

5/7/31 (Item 31 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006760149 BIOSIS NO.: 198988075264
FASTING PLASMA C-PEPTIDE **GLUCAGON** STIMULATED PLASMA C-PEPTIDE AND URINARY C-PEPTIDE IN RELATION TO CLINICAL TYPE OF **DIABETES**
AUTHOR: GJESSING H J (Reprint); MATZEN L E; FABER O K; FROLAND A
AUTHOR ADDRESS: SVANEVEJ 5, DK-5690 TOMMERUP, DENMARK**DENMARK
JOURNAL: Diabetologia 32 (5): p305-311 **1989**
ISSN: 0012-186X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Many patients with **Type 2** (non-insulin-dependent) **diabetes** mellitus are **treated** with insulin in order to control hyperglycaemia. We studied fasting plasma C-peptide, **glucagon** stimulated plasma C-peptide, and 24 h urinary C-peptide in

relation to clinical type of **diabetes** in 132 insulin **treated** diabetic subjects. Patients were classified clinically as Type 1 (insulin-dependent) diabetic subjects in the presence of at least two of the following criteria: 1) significant ketonuria, 2) insulin **treatment** started within one year after diagnosis, 3) age of diagnosis .ltoreq. 40 years, and 4) weight below 110% of ideal weight of the same age and sex. Eighty patients were classified as Type 1 and 52 as **Type 2** diabetic subjects. A second classification of patients into 6 C-peptide classes was then performed. Class I consisted of patients without islet B-cell function. Class II-VI had preserved islet B-cell function and were separated according to the 20%, 40%, 60% and 80% C-peptide percentiles. The two classifications of patients were compared by calculating the prevalence of clinical Type 1 and **Type 2 diabetes** in each of the C-peptide classes. This analysis showed that patients with a fasting plasma C-peptide value < 0.20 mmol/l, a **glucagon** stimulated plasma C-peptide value < 0.32 nmol/l, and a urinary C-pepitde value < 3.1 nmol/l, or < 0.54 nmol/mmol creatinine/24 h, or < 5.4 nmol/24 h mainly were Type 1 diabetic patients; while patients with C-peptide levels above these values mainly were **Type 2**. At these limits the percentage, predictive value of positive tests as indicators of **Type 2 diabetes** were as follows: fasting-peptide 83%, stimulated C-peptide 86%, and urinary C-peptide expressed as nmol/l 76%, as nmol/mmol creatinine/24 h 79%, and as nmol/24 h 78%. Similarly, the percentage predictive value of negative tests as indicators of Type 1 **diabetes** were as follows: fasting C-peptide 86%, stimulated C-peptide 88%, and urinary C-peptide expressed as nmol/l 79%, as nmol .cntdot. mmol creatinine .cntdot. 24 h 81%, and as nmol/24h 80%. If patients without detectable C-peptide were excluded, the predictive value of negative tests were as follows: fasting C-peptide 81%, stimulated C-peptide 88%, urinary C-peptide expressed as nmol/l 61%, as nmol/mmol creatinine/24 h 69%, and as nmol/24 h 64%. In conclusion, post **glucagon** C-peptide gives a good distinction between Type 1 and **Type 2 diabetes** mellitus in insulin **treated** **diabetes** while 24 h urinary C-peptide gives a less sensitive distinction between the clinical types of **diabetes**.

5/7/32 (Item 32 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006714711 BIOSIS NO.: 198988029826
INSULIN SECRETION AND GLUCOSE TOLERANCE IN NON-INSULIN DEPENDENT DIABETIC PATIENTS AFTER CHRONIC NIFEDIPINE **TREATMENT**
AUTHOR: TENTORIO A (Reprint); GHILARDI G; PEDRONCELLI A; BENCO R; STROPPA S ; ADIB S; GIANOLA D; PAGANI G
AUTHOR ADDRESS: DEP ENDOCRINOL, UNITED HOSP, LARGO BAROZZI, 1, I-24100-BERGAMO, ITALY**ITALY
JOURNAL: European Journal of Clinical Pharmacology 36 (3): p311-314 **1989**
ISSN: 0031-6970
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of nifedipine 40 mg .cntdot. day-1 for 3 months on glucose tolerance, insulin and C-peptide secretion after an oral glucose tolerance test (OGTT), intravenous glucose tolerance test (IVGTT) and **glucagon** stimulatory test, has been studied in 8 moderately hypertensive women suffering from non-insulin dependent **diabetes** mellitus (**NIDDM**). No significant variation in glucose metabolism was noted after nifedipine **treatment**, except for a slight

improvement in insulin secretion after OGTT at the end of the study. There was an increase in cholesterol as acollateral effect.

5/7/33 (Item 33 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006676734 BIOSIS NO.: 198987124625
RESIDUAL B CELL FUNCTION IN PATIENTS WITH LONG-STANDING **NIDDM** AND ITS RELATION TO METABOLIC CONTROL AND DIABETIC COMPLICATIONS
AUTHOR: IWASE M (Reprint); KIKUCHI M; NUNOI K; MAKI Y; WAKISAKA M; WADA M; FUJISHIMA M
AUTHOR ADDRESS: SECOND DEP INTERNAL MED, FAC MED, KYUSHU UNIV, 3-1-1 MAIDASHI, HIGASHI-KU, FUKUOKA 812, JPN**JAPAN
JOURNAL: Endocrinologia Japonica 35 (6): p803-808 **1988**
ISSN: 0013-7219
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We have evaluated the residual pancreatic B cell fusion by **glucagon** load test in 28 patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) of a duration of 20 years or more. The increase in serum C-peptide at 6 miutes after **glucagon** administration (.DELTA.C-peptide) was used as an index of residual B cell function. There was much less .DELTA.C-peptide in patients **treated** with insulin than in those **treated** with sulfonylurea ($p < 0.05$), and it was significantly correlated with the body mass index ($r = 0.40$, $p < 0.05$). Long term metabolic control assessed by the average annual mean fasting blood glucose for the observation period (mean, 21 years) was not correlated with .DELTA.C-peptide ($r = -0.13$). The prevalence of retinopathy which needed photocoagulation therapy and of neuropathy in patients with poor residual B cell function (.DELTA.C-peptide .ltoreq. 0.3 ng/ml) was the same as that in those with good residual B cell function (.DELTA.C-peptide .gtoreq. 1.0 ng/ml). The present study shows that the residual B cell function is not correlated with long term glycemic control and the prevalence of diabetic complications in long-standing **NIDDM** patients.

5/7/34 (Item 34 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006615201 BIOSIS NO.: 198987063092
CLINICAL BENEFITS AND MECHANISMS OF A SUSTAINED RESPONSE TO INTERMITTENT INSULIN THERAPY IN **TYPE 2** DIABETIC PATIENTS WITH SECONDARY DRUG FAILURE
AUTHOR: YKI-JARVINEN H (Reprint); ESKO N; EERO H; MARJA-RIITTA T
AUTHOR ADDRESS: CLINICAL DIABETES NUTRITION SECT, NIH, 4212 NORTH 16TH ST, PHOENIX, ARIZ 85016, USA**USA
JOURNAL: American Journal of Medicine 84 (2): p185-192 **1988**
ISSN: 0002-9343
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: To test the hypothesis that short-term insulin therapy may induce long-lasting metabolic improvements in patients with **type 2** **diabetes** resistant to oral therapy, 19 patients were studied before and four weeks after insulin therapy, and again four weeks after

resumption of oral medication. The mechanisms associated with changes of glycemic control after discontinuation of insulin therapy were also evaluated. During insulin therapy, blood glucose levels (228 .+-. 13 versus 123 .+-. 18 mg/dl, p < 0.001) and the basal production rate (P < 0.001) decreased, and the insulin secretory response to **glucagon** at a standardized glucose level, insulin action **in vivo**, and insulin binding and action in vitro in fat cells improved significantly. During the postinsulin oral therapy, blood glucose levels increased (194 .+-. 11 mg/dl, p < 0.001) but remained below pre-insulin **treatment** values (p < 0.01). The mean daily glucose concentration after post-insulin oral therapy correlated with the initial pre-insulin therapy glucose concentration (r = 0.83, p < 0.001). The improved rate of **in vivo** glucose disposal and the enhanced insulin secretory response persisted during oral therapy whereas the basal glucose production rate returned to its pre-insulin therapy value. It is concluded that patients with **type 2 diabetes** in whom oral therapy falls show favorable responses to insulin therapy. After discontinuation of insulin therapy, blood glucose concentrations tend to return of their individual initial values. Therefore, most of these patients require long-term insulin therapy. The mechanism behind the change of glycemic control after cessation of insulin therapy seems to be an increase in the basal glucose production rate rather than deterioration of extrahepatic insulin action or the insulin secretory response.

5/7/35 (Item 35 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006250675 BIOSIS NO.: 198886090596
IMPROVED BETA CELL FUNCTION AFTER INTENSIVE INSULIN **TREATMENT** IN SEVERE NON-INSULIN-DEPENDENT **DIABETES**
AUTHOR: GLASER B (Reprint); LEIBOVICH G; NESHER R; HARTLING S; BINDER C; CERASI E
AUTHOR ADDRESS: DEP ENDOCRINOL METABOLISM, HADASSAH UNIV HOSP, PO BOX 12 000, JERUSALEM, ISRAEL 91120**ISRAEL
JOURNAL: Acta Endocrinologica 118 (3): p365-373 **1988**
ISSN: 0001-5598
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: In **Type II**, non-insulin-dependent **diabetes**, insulin secretion is often reduced to the point where oral hypoglycaemic agents fail to control the plasma glucose level. We studied 12 patients (age 41-66 years; 4 lean, 8 obese) with **Type II** **diabetes** mellitus for 1-25 years who were uncontrolled despite maximal dose glibenclamide and metformin. After withdrawal of medication, blood glucose control was determined by measuring glucose before and 2 h after each meal for 48 h, and beta-cell function by insulin or C-peptide response to **glucagon** and to iv glucose. Following these tests, intensive insulin **treatment** (CSII) was initiated, and near-euglycaemia (mean of 7 daily glucose determinations < 7.7 mmol/l) was maintained for 16.6 .+-. 1.5 days, at which time the tests were repeated. Mean daily insulin requirement was 61 .+-. 9 IU (0.81 .+-. 0.09 IU/kg). Glucose control was improved after cessation of CSII (mean glucose 12.7 .+-. 0. 6 mmol/l after vs 20 .+-. 1.5 mmol/l before, P < 0.005). Maximum incremental C-peptide response improved both to **glucagon** (214 .+-. 32 after vs 134 .+-. 48 pmol/l before, P = 0.05) and to glucose iv bolus injection (284 .+-. 53 vs 113 .+-. 32 pmol/l, P < 0.05). Peak insulin response, measured after iv glucose infusion, also

tended to be higher in the post-CSII test (42 .+-. 18 vs 22 .+-. 5.6 mU/l). Basal and stimulated proinsulin concentrations were high relative to C-peptide levels during the pre-**treatment** period, but returned to normal after CSII. Thus: 1) adequate blood glocose control could be obtained in most of our patients using moderate doses of insulin even in those who were obese; 2) short-term euglycaemia resulted in improved insulin response to both **glucagon** and glucose, and reduction of the relative proinsulin secretion; 3) although beta-cell function improved in most patients, only 6 could be adequately controlled with oral agents after hospital discharge. In those patients who do not respond well to conventional **treatment**, CSII is an attractive alternative.

5/7/36 (Item 36 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006217928 BIOSIS NO.: 198886057849
PHYSIOLOGICAL IMPORTANCE OF DEFICIENCY IN EARLY PRANDIAL INSULIN SECRETION IN NON-INSULIN-DEPENDENT **DIABETES**
AUTHOR: BRUCE D G (Reprint); CHISHOLM D J; STORLIEN L H; KRAEGEN E W
AUTHOR ADDRESS: GARVAN INST MED RES, ST VINCENT'S HOSP, DARLINGHURST, NSW 2010, AUST**AUSTRALIA
JOURNAL: Diabetes 37 (6): p736-744 **1988**
ISSN: 0012-1797
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) have a deficiency in early prandial insulin secretion. To determine the contribution of this early deficiency to prandial hyperglycemia, exogenous intravenous insulin (1.8 U over 30 min) was delivered to eight **NIDDM** subjects in a profile designed to simulate the normal initial rise in insulin levels. The same dose of insulinm was also **administered** (1) in the same profile but delayed by 30 min and (2) as a constant infusion over 180 min. Augmentation of the early insulin response caused a 33 .+-. 4% reduction in the glycemic response to a mixed meal (P < .005); the peak blood glucose increment above baseline was reduced by 1.4 mM (P < .005) to an increment identical to nondiabetic subjects (3.3 .+-. 0.3 vs. 3.2 .+-. 0.2 mM), and blood glucose levels were still 0.9 mM lower after 180 min (P < .05). In contrast, the delayed profile or constant infusion did not significantly alter the glycemic response to the meal. Early insulin augmentation resulted in elevated peripheral insulin levels initially (peak level 81 .+-. 11 mU/L), but subsequent insulin and C-peptide levels were lower than in the control study (at 180 min after the meal, 22 .+-. 5 vs. 33 .+-. 8 mU/L, P < .05, and 4.0 .+-. 0.5 vs. 5.3 .+-. 0.6 .mu.g/L, P < .02, respectively). Early insulin delivery caused free-fatty acid (FFA) levels to fall at a faster rate after the meal and also attenuated the initial rise in **glucagon** levels typical of **NIDDM**. We conclude that the deficiency in early prandial insulin secretion contributes to prandial hyperglycemia and late hyperinsulinemia and may be partially responsible for the abnormal FFA and **glucagon** responses in **NIDDM**.

5/7/37 (Item 37 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006196839 BIOSIS NO.: 198886036760

ADVERSE METABOLIC EFFECT OF OMEGA-3 FATTY ACIDS IN NON-INSULIN-DEPENDENT **DIABETES** MELLITUS
AUTHOR: GLAUBER H (Reprint); WALLACE P; GRIVER K; BRECHTEL G
AUTHOR ADDRESS: BEAVERTON, OREG 97005, USA**USA
JOURNAL: Annals of Internal Medicine 108 (5): p663-668 **1988**
ISSN: 0003-4819
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Increased interest in using omega-3 fatty acids led us to examine their metabolic effects in six men with **type II** (non-insulin-dependent) **diabetes** mellitus. After 1 month of a diet supplemented with these fatty acids, the patients' fasting glucose rose from 13.1 .+-. 1.3 to 15.3 .+-. 1.3 mmol/L (P=0.03) and glucose area duing a mixed meal profile rose by 22% (P=0.04). Basal hepatic glucose output rose from 97 .+-. 9 to 122 .+-. 8 mg/m2 .cntdot. min (P=0.004) but glucose disposal rates measured by euglycemic glucose clamp were unchanged. Fasting insulin levels were similar; peak insulin levels stimulated by meals or intravenous **glucagon** fell by 30% and 39%, respectively. Plasma and erythrocyte content of omega-3 fatty acid arose significantly. After omega-3 fatty acid withdrawal, fasting glucose returned to baseline. Omega-3 fatty acid **treatment** in **type II diabetes** leads to rapid but reversible metabolic deterioration, with elevated basal hepatic glucose output and impaired insulin secretion but unchanged glucose disposal rates. Caution should be used when recommending omega-3 fatty acids in **type II** diabetic persons.

5/7/38 (Item 38 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006120056 BIOSIS NO.: 198885088947
COUNTERREGULATION IN **TYPE 2** NON-INSULIN-DEPENDENT **DIABETES** MELLITUS NORMAL ENDOCRINE AND GLYCEMIC RESPONSES UP TO TEN YEARS AFTER DIAGNOSIS
AUTHOR: HELLER S R (Reprint); MACDONALD I A; TATTERSALL R B
AUTHOR ADDRESS: DEP MED, C FLOOR, SOUTH BLOCK, UNIV HOSP, QUEEN'S MED CENT, NOTTINGHAM NG7 2UH, UK**UK
JOURNAL: Diabetologia 30 (12): p924-929 **1987**
ISSN: 0012-186X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We have examined hormonal and metabolic responses to insulin-induced hypoglycaemia in 10 **Type 2** (non-insulin-dependent) diabetic patients **treated** with tablets and 10 age, sex and weight matched control subjects. Diabetic patients were under 110% ideal body weight, had no autonomic neuropathy and were well controlled (HbA1, 7.1 .+-. 0.2%). After the diabetic patients were kept euglycaemic by an overnight insulin infusion, hypoglycaemia was induced in both groups by intravenous insulin at 30 mU .cntdot. m-2 .cntdot. min-1 for 60 min and counterregulatory responses measured for 150 min. There were no significant differences between diabetic patients and control subjects in the rate of fall (3.3 .+-. 0.3 vs 4.0 .+-. 0.3 mmol .cntdot. l-1 .cntdot. h-1), nadir (2.4 .+-. 0.2 vs 2.3 .+-. 0.1 mmol/l) and rate of recovery (0.027 .+-. 0.002 vs 0.030 .+-. 0.003 mmol .cntdot. l-1 .cntdot. min-1) of blood glucose. Increments of **glucagon** (60.5 .+-. 5.7 vs 70 .+-. 9.2 ng/l) and adrenaline (1.22 .+-. 0.31 vs 1.45 .+-.

0.31 nmol/l) were similar in both groups. When tested using this model, patients with **Type 2 diabetes**, without microvascular complications and taking oral hypoglycaemic agents show no impairment of the endocrine response and blood glucose recovery following hypoglycaemia.

5/7/39 (Item 39 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006110451 BIOSIS NO.: 198885079342
ORGAN-SPECIFIC AUTOIMMUNITY AND HLA-DR ANTIGENS AS MARKERS FOR BETA CELL DESTRUCTION IN PATIENTS WITH **TYPE II DIABETES**
AUTHOR: GROOP L (Reprint); MIETTINEN A; GROOP P-H; MERI S; KOSKIMIES S; BOTTAZZO G F
AUTHOR ADDRESS: FOURTH DEP MED, HELSINKI UNIV CENTRAL HOSP, UNIONINKATU 38, SF-00170 HELSINKI, FINLAND**FINLAND
JOURNAL: Diabetes 37 (1): p99-103 **1988**
ISSN: 0012-1797
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Islet cell antibodies (ICAs), thyrogastric antibodies, and HLA-DR antigens were determined in 204 patients with **type II** (non-insulin-dependent) **diabetes** controlled with diet and/or oral hypoglycemic agents (NIR) and in 108 age-matched patients who require insulin to control their hyperglycemia (IR). .beta.-Cell function measured as C-peptide response to **glucagon** was evaluated in relation to the presence of ICAs and HLA-DR antigens. The IR patients differed from the NIR patients with respect to higher frequency of ICAs ($P < .001$), thyroid antibodies ($P < .02$), and the HLA antigen DR4 ($P < .02$). The highest frequency of ICAs and thyroid antibodies was observed in female insulin-**treated** subjects (51.2 and 46.4%). Patients who were heterozygous for HLA-DR3/DR4 showed significantly higher frequency of ICAs ($P < .01$) and complement-fixing ICAs ($P < .001$) than patients without the heterozygous form DR3/DR4. Neither the presence of ICA alone nor DR3/DR4 alone was associated with a significant impairment of .beta.-cell function. However, when both ICA and DR3/DR4 were present in a diabetic individual, .beta.-cell function was markedly impaired ($P < .001$), suggesting that both genetic and autoimmune factors are necessary to facilitate the process leading to .beta.-cell destruction of the patients. Our findings suggest that **type II diabetes** is a heterogeneous disorder including at least two major subgroups, which can be further characterized by HLA-DR antigens and organ-specific antibodies.

5/7/40 (Item 40 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006098394 BIOSIS NO.: 198885067285
PLASMA C PEPTIDE LOW RESPONDERS DURING **GLUCAGON** TEST HETEROGENEITY IN **DIABETES** FROM THE VIEW POINT OF PLASMA C PEPTIDE RESPONSES TO **GLUCAGON** AND ARGININE
AUTHOR: SANKE T (Reprint); SOWA R; HANABUSA T; MORITA H; TABATA H; KUBO K; KONDO M; NANJO K; MIYAMURA K
AUTHOR ADDRESS: FIRST DEP MED, WAKAYAMA UNIV MEDICAL SCIENCE, 1-7 BANCHO, WAKAYAMA 640, JPN**JAPAN
JOURNAL: Journal of the Japan Diabetes Society 30 (9): p795-802 **1987**

ISSN: 0021-437X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: The characteristics of insulin secretory capabilities in low responders for plasma C-peptide (CPR) after **glucagon** injection were studied in relation to the disease classification of **diabetes** mellitus (DM). The subjects consisted of 50 low responders who showed less than 0.5 ng/ml of .DELTA.G (the increase from basal plasma CPR levels 5 min after 1 mg **glucagon**, iv), 128 **type II** diabetics (**type II** DM group) who showed more than 0.6 ng/ml of .DELTA.G, and nine normal controls (N group). The low responders were composed of 15 type I diabetics with disease of more than two years' duration (Ia group), seven patients with type I DM of the early stage (Ib group), 19 insulin-**treated** patients with **type II** DM (IIa group), and nine non-insulin-**treated type II** diabetics (IIb group). The subjects were injected intravenously with 4 g arginine, and .DELTA.A (the increase from basal plasma CPR five min after arginine) was obtained to calculate .DELTA.G/.DELTA.A. Both .DELTA.G and .DELTA.A in the **type II** DM group were lower than in the N group, while there was no appreciate difference in .DELTA.G/.DELTA.A between the two groups. In almost all of the Ia group and some of the IIa group, both .DELTA.G and .DELTA.A were too low to calculate .DELTA.G/.DELTA.A. On the other hand, .DELTA.G in the Ib and IIb groups was markedly low; however, .DELTA.A was relatively retained and .DELTA.G/.DELTA.A in these groups was significantly low compared with that in both **type II** and N groups. The IIb group possessed HLA (DR loci) similar to that of type I DM and two of them became insulin dependent at a later stage. These findings strongly suggest the possibility that patients with low levels of .DELTA.G/.DELTA.A in **type II** DM have a condition similar to type I DM.

5/7/41 (Item 41 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006061535 BIOSIS NO.: 198885030426
GLUCAGON-C-PEPTIDE TEST AS A MEASURE OF INSULIN REQUIREMENT IN **TYPE 2 DIABETES** EVALUATION OF STOPPING INSULIN THERAPY IN ELEVEN PATIENTS
AUTHOR: VIIKARI J (Reprint); RONNEMAA T; KOSKINEN P
AUTHOR ADDRESS: DEP MED, UNIV CENTRAL HOSP, SF-20520 TURKU, FINL**FINLAND
JOURNAL: Annals of Clinical Research 19 (3): p178-182 **1987**
ISSN: 0003-4762
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The **glucagon** C-peptide test was evaluated as a predictor of the requirement of insulin therapy in **type 2 diabetes** mellitus. Endogenous insulin secretory capacity was measured in a population of 150 insulin-**treated** adult diabetic patients by determining postprandial **glucagon**-stimulated plasma C-peptide concentration (Novo, antiserum M 1230). Eleven subjects with C-peptide levels above 1.0 nmol/l comprised the subgroup in which the previously started insulin therapy was discontinued. After an observation period of a week in hospital the metabolic control of the patients was followed in an outpatient clinic for twelve months. During the observation period one patient was managed on diet alone, eight subjects required oral hypoglycaemics agents and two required the reinstitution of insulin

therapy. Mean fasting blood glucose and GHbA1 (glycosylated haemoglobin) of non-insulin dependent diabetics increased during the observation period (from 8.8 to 11.8 mmol/l, $p < 0.001$, and from 12.2 to 14.1%, $p < 0.05$, respectively). No significant changes were found in total or HDL-cholesterol or triglyceride levels. The findings demonstrate that the **glucagon**-C-peptide test can be used as an aid in judging whether the withdrawal of insulin may be considered without excessive risk of developing diabetic ketoacidosis. However, the test cannot be used as the only criterion when assessing the need for exogenous insulin in **type 2 diabetes**. Meticulous monitoring of blood glucose levels is necessary when insulin therapy is withdrawn, because diabetic patients with peripheral insulin resistance may not maintain satisfactory glycaemic controlwithout exogenous insulin despite of high residual endogenous insulin secretion.

5/7/42 (Item 42 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0006034411 BIOSIS NO.: 198885003302
FAMILIAL **DIABETES** MELLITUS WITH VARIABLE B CELL RESERVE ANALYSIS OF A PEDIGREE
AUTHOR: BODANSKY H J (Reprint); KELLY W F
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JOURNAL: Diabetologia 30 (8): p638-640 **1987**
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RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Some patients do not fall neatly into the categories of Type 1 (insulin-dependent), **Type 2** (non-insulin-dependent) or maturity onset **diabetes** of young people **diabetes**. The pedigree and characteristics of the family reported here illustrate this problem. Nine cases of **diabetes** are known in 4 out of 5 generations, with onset between 17-70 years. **Treatment** was with insulin in 5 (onset 17-29 years), tablets in 3 (onset 32-70 years), and in one **diabetes** occurred before the insulin era. Plasma C-peptide was 0.04-0.52 nmol/l (fasting) and 0.35-1.33 nmol/l (peak stimulation with **glucagon**). HLA typing, available in 7 diabetic patients showed DR2 or DR7 in all, DR4 in 2 and DR3 in none. Pancreatic islet cell antibodies were absent at diagnosis in the most recently diagnosed patient. Diabetic complications remain absent in two insulin-**treated** patients (duration 28 and 24 years), but have occurred extensively in the remainder. The form of **diabetes** in this family is therefore characterised by (a) strong family history (possible autosomal dominant with variable penetrance), (b) widely variable age of onset, (c) a variable degree of B cell reserve (d) no association with HLA DR3/4 and the presence of DR2 or DR7 and (e) no protection from complications.

5/7/43 (Item 43 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005757415 BIOSIS NO.: 198784111564
PANCREATIC BETA CELL FUNCTION IN NON-INSULIN-DEPENDENT **DIABETES** MELLITUS DURING SUCCESSIVE PERIODS OF SULFONYLUREA AND INSULIN **TREATMENT** SERUM C-PEPTIDE RESPONSE TO **GLUCAGON** AND URINE

C-PEPTIDE EXCRETION
AUTHOR: HSIEH S D (Reprint); IWAMOTO Y; MATSUDA A; KUZUYA T
AUTHOR ADDRESS: DIV ENDOCRINOLOGY METABOLISM, JICHI MED SCH, MINAMIKAWACHI-MACHI, TOCHIGI-KEN, 329-04, JAPAN**JAPAN
JOURNAL: Endocrinologia Japonica 34 (4): p561-568 **1987**
ISSN: 0013-7219
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Serum C-peptide responses to **glucagon** and daily urine C-peptide excretion in successive periods of different **treatment** in two groups of patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) (mean interval between two tests < 1 month) were compared. In group A patients (n = 8), the glycemic control was improved after transferring the **treatment** from sulfonylurea (SU) to insulin (fasting plasma glucose: SU: 192 .+-. 47, insulin: 127 .+-. 21 mg/dl, mean .+-. S.D., p < 0.01). Fasting serum C-peptide immunoreactivity (CPR) was significantly lower at the period of insulin **treatment** (SU: 1.93 .+-. 1.01, insulin: 1.47 .+-. 0.79 ng/ml, p < 0.05), but there was no difference in the increase in serum CPR (maximal-fasting) (.DELTA. serum CPR) during **glucagon** stimulation in the two periods of **treatment** (SU: 1.70 .+-. 0.72, insulin: 1.47 .+-. 0.98 ng/ml). In group B patients (n = 7), there was no significant difference in glycemic control after transferring the **treatment** from insulin to SU (fasting plasma glucose: insulin: 127 .+-. 24, SU: 103 .+-. 13 mg/dl). Fasting serum CPR was significantly lower during the period of insulin **treatment** (insulin: 1.39 .+-. 0.64, SU: 2.21 .+-. 0.86 ng/ml, p < 0.025), but .DELTA. serum CPR during **glucagon** stimulation still showed no significant difference between the two periods (insulin: 1.97 .+-. 1.16, SU: 2.33 .+-. 1.57 ng/ml). On the other hand, daily urine CPR excretion was constantly lower during insulin **treatment** than during SU **treatment** in both groups (group A: SU: 65.6 .+-. 23.2, insulin: 37.1 .+-. 15.3 .mu.g, p < 0.01, group B: insulin: 40.3 .+-. 14.7, SU: 65.6 .+-. 12.4 .mu.g, p < 0.01). The data suggest that basal and daily pancreatic B-cell secretion in **NIDDM** patients varies within the short periods of different **treatment**. However, the CPR response to **glucagon** remains stable.

5/7/44 (Item 44 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005756823 BIOSIS NO.: 198784110972
DIETARY SUGARS AND CARBOHYDRATE METABOLISM IN **TYPE II DIABETES**
AUTHOR: HALLFRISCH J (Reprint)
AUTHOR ADDRESS: GERONTOL RES CENT, NATL INST HEALTH, FRANCIS SCOTT KEY MED CENT, BALTIMORE, MD 21224, USA**USA
JOURNAL: Journal of the American College of Nutrition 6 (5): p385-396 **1987**
ISSN: 0731-5724
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: **Diabetes**, the most common metabolic disease, is responsible for the deaths of over 300,000 Americans annually. The incidence of the disease increases with age and since the U.S. population is graying, prevalence is also increasing. Obesity and family history are strong predictors of **diabetes**. The etiology of **Type II**

diabetes is heterogeneous. The hyperglycemia of **Type II diabetes** can result from a variety of metabolic defects including impaired .beta. cell secretion, receptor deficiencies, or abnormal hepatic production or uptake of glucose. Other glucoregulatory hormones such as **glucagon**, growth hormone, cortisol, thyroid hormones, somatostatin, and gastric inhibitory polypeptide may contribute to the aberrations of carbohydrate metabolism. Environmental factors including stress, diet, and exercise may also contribute to the disease. Since most diabetics are obese, weight loss should be the first priority in improving status. A variety of diet and exercise regimens may help achieve this goal or even improve glucose control without weight loss. Due to the heterogeneity of the disease individualized **treatment** must be used to improve status of patients with the various metabolic defects of **Type II diabetes**.

5/7/45 (Item 45 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005705076 BIOSIS NO.: 198784059225
ANTIHYPERTENSIVE GUANFACIN THERAPY IN PATIENTS WITH **TYPE II DIABETES** MELLITUS
AUTHOR: COVES M J (Reprint); GOMIS R; GODAY A; CASAMITJANA R; RIVERA F; VILARDELL E
AUTHOR ADDRESS: SERV DE ENDOCRINOL DIABETES, HOSP CLIN PROVINCIAL, C/VILLARROEL, 17008036 BARCELONA**SPAIN
JOURNAL: Medicina Clinica 88 (8): p315-317 **1987**
ISSN: 0025-7753
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: SPANISH

ABSTRACT: The antihypertensive effect of guanfacine was studied in 20 patients with **type II diabetes** mellitus. Guanfacine is an alpha-adrenoceptor agonist on insulin secretion, and it has been suggested that the latter could be altered by the drug through adenyl-cyclase inhibition. The results showed that antihypertensive therapy with guanfacine did not modify the beta pancreatic function in patients with **type II diabetes** mellitus, as measured by the response of C-peptide to intravenous **glucagon** challenge. It was also shown that the level of glycosilated hemoglobin was not modified by the **treatment**. It is concluded that guanfacine may be an adequate drug for the therapy of hypertension in patients with **type II diabetes** mellitus, since it does not modify insulin secretion or the metabolic control of the latter disease.

5/7/46 (Item 46 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005695460 BIOSIS NO.: 198784049609
NO EFFECT OF GLICLAZIDE ON GASTRIC INHIBITORY POLYPEPTIDE GIP IN **TYPE II DIABETES**
AUTHOR: SCOTT R S (Reprint); DONNELLY T
AUTHOR ADDRESS: DEP MED, CHRISTCHURCH SCH MED, CHRISTCHURCH, NEW ZEALAND** NEW ZEALAND
JOURNAL: Diabetes Research and Clinical Practice 3 (3): p175-178 **1987**
ISSN: 0168-8227
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Seven subjects with non-insulin-dependent **diabetes** mellitus were studied prior to and after 1 month of **treatment** with gliclazide, 80 mg twice daily. Individuals attended for a standard breakfast test meal (10 kcal/kg) on three occasions - prior to therapy, first day of therpy, and 30th day of therapy. Blood samples were collected between 0 and 240 min post-prandially and assayed for glucose, insulin, C-peptide, **glucagon**, pancreatic polypeptide, gastric inhibitory polypeptide (GIP), and gastrin. Following gliclazide, fasting and post-prandial glucose levels were significantly improved. An increase in post-prandial insulin and C-peptide levels was noted on the first **treatment** day and values remained elevated for the study period. GIP and other measured peptide hormones were unchanged. These data suggest that gliclazide asserts its hypoglycaemic effects by promoting insulin release, and has no detectable effect on other enteropancreatic hormones.

5/7/47 (Item 47 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005674179 BIOSIS NO.: 198784028328
EFFECT OF GLYBURIDE ON GLYCEMIA CONTROL INSULIN REQUIREMENT AND GLUCOSE METABOLISM IN INSULIN-**TREATED** DIABETIC PATIENTS
AUTHOR: SIMONSON D C (Reprint); DELPRATO S; CASTELLINO P; GROOP L; DEFRONZO R A
AUTHOR ADDRESS: SEC ENDOCRINOL, DEP INTERNAL MED, YALE UNIV SCH MED, 333 CEDAR ST, NEW HAVEN, CONN 06510, USA**USA
JOURNAL: Diabetes 36 (2): p136-146 **1987**
ISSN: 0012-1797
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Glycemic control and glucose metabolism were examined in 5 patients with insulin-dependent **diabetes** mellitus (IDDM) and 8 insulin-**treated** non-insulin-dependent **diabetes** mellitus (**NIDDM**) patients before and after 2 mo of therapy with glyburide (20 mg/day). Glycemic control was assessed by daily insulin requirement, 24-h plasma glucose profile, glucosuria, and glycosylated hemoglobin. Insulin secretion was evaluated by **glucagon** stimulation of C-peptide secretion, and insulin sensitivity was determined by a two-step euglycemic insulin clamp (1 and 10 mU .cntdot. kg-1 .cntdot. min-1) performed with indirect calorimetry and [3-3H]glucose. In the IDDM patients, the addition of glyburide produced no change in daily insulin dose (54 .+-. 8 vs. 53 .+-. 7 U/day), mean 24-h glucose level (177 .+-. 20 vs. 174 .+-. 29 mg/dl), glucosuria (20 .+-. 6 vs. 35 .+-. 12 g/day) or glycosylated hemoglobin (10.1 .+-. 1.0 vs. 9.5 .+-. 0.7%). Furthermore, there was no improvement in basal hepatic glucose production (2.1 .+-. 0.2 vs. 2.4 .+-. 0.1 mg .cntdot. kg-1 .cntdot. min-1), suppression of hepatic glucose production by low- and high-dose insulin infusion, or in any measure of total, oxidative, or nonoxidative glucose metabolism in the basal state or during insulin infusion. C-peptide levels were undetectable (< 0.01 pmol/ml) in the basal state and after **glucagon** infusion and remained undetectable after glyburide therapy. In contrast to the IDDM patients, the insulin-**treated NIDDM** subjects exhibited significant reductions in daily insulin requirement (72 .+-. 6 vs. 58 .+-. 9 U/day), mean 24-h plasma glucose concentration (153 .+-. 10 vs. 131 .+-. 5 mg/dl), glucosuria (14 .+-. 5 vs. 4 .+-. 1 g/day), and

glycosylated hemoglobin (10.3 .+-. 0.7 vs. 8.0 .+-. 0.4%) after glyburide **treatment** (all P .ltoreq. .05). However, there was no change in basal hepatic glucose production (1.7 .+-. 0.1 vs. 1.7 .+-. 0.1 mg .cntdot. kg-1 .cntdot. min-1), suppression of hepatic glucose production by insulin, or insulin sensitivity during the two-step insulin-clamp study. Both basal (0.14 .+-. 0.05 vs. 0.32 .+-. 0.05 pmol/ml, P < .05) and **glucagon**-stimulated (0.24 .+-. 0.07 vs. 0.44 .+-. 0.09 pmol/ml) C-peptide levels rose after 2 mo of glyburide therapy and both were correlated with the decrease in insulin requirment (basal: r = .65, P = .08; **glucagon** stimulated: r = .93, P < .001). These data indicate that in IDDM subjects, the addition of glyburide to insulin does not affect insulin requirement, glycemic control, or insulin sensitivity. In contrast, in insulin-**treated NIDDM** patients, glyburide produces a modest decrease in insulin dose and improves glycemic control without altering insulin sensitivity. This improvment in glucose metabolism primarily reflects an increase in endogenous insulin secretion.

5/7/48 (Item 48 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005674178 BIOSIS NO.: 198784028327
INITIAL PHASE II CLINICAL STUDIES ON MIDAGLIZOLE DG-5128 A NEW HYPOGLYCEMIA AGENT
AUTHOR: KAWAZU S (Reprint); SUZUKI M; NEGISHI K; ISHII J; SANDO H; KATAGIRI H; KANAZAWA Y; YAMAOUCHI S; AKANUMA Y; ET AL
AUTHOR ADDRESS: FOURTH DEP INTERNAL MED, SAITAMA MED SCH, 38 MOROHONGO, MOROYAMA, IRUMA-GUN, SAITAMA, JPN 350-04**JAPAN
JOURNAL: Diabetes 36 (2): p221-226 **1987**
ISSN: 0012-1797
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Midaglizole (DG-5128), 2-[2-(4,5-dihydro-1H-imidazol-2-yl)-1-phenylethyl]pyridine dihydrochloride sesquihydrate, is a new type of oral antidiabetic agent that has an .alpha.2-adrenoceptor-antagonizing effect. As previously reported, midaglizole reduces plasma glucose, mainly by stimulation of insulin secretion, and inhibits epinephrine-induced platelet aggregation in normal human subjects. In this study, the clinical safety and efficacy of shortterm administration of midaglizole were evaluated in 47 patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**). After an observation period on diet or sulfonylurea **treatment** (1 patient was on insulin), patients received 150-250 mg 3 times a day of midaglizole for 2-4 wk, (some patients continued **treatment** for > 4 wk). In 20 of the patients first **treated** with diet and then switched to midaglizole **treatment**, fasting plasma glucose (FPG) decreased significantly from 187 .+-. 10 mg/dl (mean .+-. SE) to 147 .+-. 13 mg/dl (P < .05) and 120 .+-. 6 mg/dl (P <. 01) 2 and 4 wk, respectively, after administration of midaglizole. Glycosylated hemoglobin (HbA1) also decreased from 12.0 .+-. 0.7 to 11.3 .+-. 1.1 and 10.7 .+-. 0.6% after 2 and 4 wk, respectively. In 23 of the patients whose **treatment** was changed from sulfonylureas to midaglizole, FPG, and HbA1 levels were maintained at the same value obtained before administration of midaglizole. In patients **treated** with midaglizole for > 12 wk, FPG and HbA1 were kept at the lowered levels. Moreover, midaglizole **treatment** showed a clear inhibitory effect on postprandial hyperglycemia and on FPG, reflecting the general improvement in the daily plasma glucose curve with significantly reduced fluctuation.

In the oral glucose tolerance test, midaglizole significantly improved glucose tolerance, potentiated insulin secretion, and tended to depress **glucagon** secretion. No abnormal findings attributable to midaglizole were noted in clinical and laboratory examinations, except for diarrhea and soft stools in 4 cases (8.5%) out of 47. No hypoglycemic symptoms were observed in this trial. Thus, midaglizole is clinically effective for **NIDDM** because it improves the daily plasma glucose curve, with decreased fasting and postprandial hyperglycemia, in addition to amelioration of oral glucose tolerance accompanied by accelerated insulin secretion.

5/7/49 (Item 49 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005674136 BIOSIS NO.: 198784028285
SERUM C-PEPTIDE CONCENTRATIONS AND THEIR VALUE IN EVALUATING THE USEFULNESS OF INSULIN THERAPY IN ELDERLY DIABETICS
AUTHOR: KYLLASTINEN M (Reprint); ELFVING S
AUTHOR ADDRESS: KOSKELA HOSP, KAPYLANTIE 11, SF-00600 HELSINKI**FINLAND
JOURNAL: Gerontology 32 (6): p317-326 **1986**
ISSN: 0304-324X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Serum C-peptide concentrations were determined in 121 elderly subjects: 25 nondiabetic controls aged 69-86 years, and 96 **type 2** (noninsulin-dependent **diabetes** mellitus) diabetics aged 64-96 years. Forty-seven of the diabetics were **treated** with tablets, 35 with insulin, and 14 with diet alone. Fasting serum C-peptide concentrations (nmol/l; means .+-. SD) were 0.51 .+-. 0.20 for controls; 0.60 .+-. 0.16 for diabetics on diet alone; 0.72 .+-. 0.33 for diabetics on tablets and 0.46 .+-. 0.23 diabetics on insulin ($p < 0.001$ for diabetics on tablets vs. controls and diabetics on tablets vs. diabetics on insulin). The **glucagon**-stimulated C-peptide concentrations were similar in all groups; the increment after **glucagon** was less in the diabetic patients on tablets or on insulin than in the nondiabetics. In 10 patients on insulin **treatment** and with fasting C-peptide of 0.24-1.46 nmol/l an attempt was made to withdraw insulin. In 4 subjects the transfer to tablets was possible. Serum C-peptide level did not predict the outcome of the attempt to change the therapy, but the possibility of an adequate dietary regimen seemed to be important. The results demonstrate a wide range of basal C-peptide concentrations in elderly diabetics on different **treatments**, which may indicate varying pathogenetic contributions of insulin deficiency and resistance in these patients. Our observations emphasize the necessity for regular re-evaluation of the therapeutic management of elderly diabetic patients.

5/7/50 (Item 50 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005649058 BIOSIS NO.: 198784003207
PANCREATIC BETA-CELL SECRETION AFTER ORAL GLUCOSE AND INTRAVENOUS **GLUCAGON** DIFFERENT RESPONSES TO DIETARY CONTROL OF PLASMA GLUCOSE IN NEWLY DIAGNOSED PATIENTS WITH **NIDDM**
AUTHOR: HSIEH S D (Reprint); IWAMOTO Y; MATSUDA A; KUZUYA T
AUTHOR ADDRESS: DIV ENDOCRINOL METABOLISM, JICHI MED SCH, MINAMIKAWACHI-MACHI, TOCHIGI-KEN 329-04, JAPAN**JAPAN

JOURNAL: Metabolism Clinical and Experimental 36 (4): p384-387 **1987**
ISSN: 0026-0495
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Pancreatic .beta.-cell secretion after oral glucose or intravenous **glucagon** stimulation was studied in newly diagnosed patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) before and after glycemic control by diet **treatment** alone. Insulin secretion to oral glucose showed significant improvement, while C-peptide release by **glucagon** showed no significant difference before and after diet **treatment**. The finding suggests that pancreatic .beta.-cell response to oral glucose varies with different metabolic states, but this is not so after **glucagon** stimulation in **NIDDM** patients.

5/7/51 (Item 51 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005649046 BIOSIS NO.: 198784003195
DISCRIMINATION OF TYPE I FROM INSULIN-**TREATED TYPE II** DIABETIC PATIENTS BY C-PEPTIDE MEASUREMENT
AUTHOR: CRAVAREZZA P (Reprint); RADAELI E; TOFFOLI C; RIGOSA C
AUTHOR ADDRESS: CATTEDRA DI PATOL MED, UNIV DI BRESCIA, BRESCIA-ITALY** ITALY
JOURNAL: Acta Diabetologica Latina 23 (4): p345-350 **1986**
ISSN: 0001-5563
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Residual B-cell function was assessed in 61 type I and 17 **type II** insulin-**treated** diabetics by measuring plasma C-peptide concentration before and after i.v. injection of 1 mg **glucagon** to evaluate a possible difference in response to the test in the two groups. Fasting and post-stimulatory C-peptide levels were significantly higher in **type II** diabetics than in type I (0.45 .+-. 0.25 vs. 0.12 .+-. 0.10 nmol/l for basal IRCP, 0.39 .+-. 0.19 vs. 0.06 .+-. 0.11 nmol/l for .DELTA.IRCP, $p < 0.0001$), but there was some overlap in individual values. Twenty-one percent of type I and 29% of **type II** diabetics had values in the overlap area. These percentages were reduced to 6% and 12%, respectively when only long-term (duration of **diabetes** more than five years) type I diabetics were considered. These data indicate that a **glucagon** test is useful to discriminate most type I diabetics from insulin **treated type II** diabetics.

5/7/52 (Item 52 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005264362 BIOSIS NO.: 198682110749
C-PEPTIDE SECRETION IN CALCIFIC TROPICAL PANCREATIC **DIABETES**
AUTHOR: VANNASAENG S (Reprint); NITIYANANT W; VICHAYANRAT A; POLYBUTR S; HARNTHONG S
AUTHOR ADDRESS: DEP OF MED, SIRIAJ HOSP, BANGKOK 10700, THAILAND**THAILAND
JOURNAL: Metabolism Clinical and Experimental 35 (9): p814-817 **1986**
ISSN: 0026-0495

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Serum C-peptide levels were measured during a **glucagon** stimulation test in ten normal nonobese controls and 54 diabetic patients with recent onset of **diabetes** under 30 years of age. Diabetic patients were comprised of 13 CTPD, 23 IDDM, and 18 **NIDDM**. As similar to IDDM patients, serum C-peptide concentration did not rise significantly ($P > 0.05$) in response to **glucagon** administration in CTPD-patients. Mean baseline and peak serum C-peptide concentrations in CTPD-patients were significantly lower ($P < 0.001$) than the values in normal controls and **NIDDM** patients, but were significantly higher ($P < 0.05$) than those in IDDM patients. We conclude that CTPD patients have partial C-peptide reserve, which may protect against ketosis and contribute to ketosis resistance in CTPD. Our results also suggest that CTPD patients require insulin **treatment**. Neither baseline nor peak C-peptide levels after **glucagon** could discriminate CTPD from IDDM and CTPD from **NIDDM**.

5/7/53 (Item 53 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005191144 BIOSIS NO.: 198682037531
GLICLAZIDE ON LONG-TERM THERAPY INCREASES INSULIN RESPONSE TO GLUCOSE OF **TYPE II DIABETES**
AUTHOR: COUTURIER E (Reprint)
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JOURNAL: Diabetes Research and Clinical Practice 1 (6): p343-348 **1985**
ISSN: 0168-8227
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Twelve **type II** diabetics were **treated** with gliclazide, a potent hypoglycaemic sulfonylurea, for 5 months. Plasma immunoreactive insulin (IRI), connecting peptide (C-peptide) and immunoreactive **glucagon** (IRG) were measured during a 2 h oral glucose tolerance test (OGTT) before and during gliclazide therapy. The OGTT improved in 7 patients. In those patients IRI concentrations were significantly more elevated during than before the **treatment** period. By contrast, gliclazide **treatment** did not affect the hepatic extraction of insulin (estimated by the molar ratio of C-peptide to IRI) nor the inappropriate **glucagon** release commonly observed in this type of patients.

5/7/54 (Item 54 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005097776 BIOSIS NO.: 198681061667
FASTING SERUM KETONE BODIES IN DIABETICS FROM THE ASPECT OF CARDIOPULMONARY RESUSCITATION RESPONSE
AUTHOR: KUBO K (Reprint); SANKE T; SATOGAMI E; KIMURA S; NOMURA Y; MORIYAMA Y; KONDO M; NANJO K; MIYAMURA K
AUTHOR ADDRESS: 1ST DEP INTERN MED, WAKAYAMA MED SCH, WAKAYAMA, JPN**JAPAN
JOURNAL: Journal of the Japan Diabetes Society 28 (10): p1113-1117

1985
ISSN: 0021-437X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: The levels of fasting serum total ketone bodies (TKB), acetoacetate(AcAc), and 3-hydroxybutyrate (3-OHB) is diabetics were determined by the diazonium method to evaluate the significance of these measurements in **diabetes** mellitus (DM). The following results were obtained: The diabetics studied were shown to have significantly higher levels of TKB, AcAc, 3-OHB and 3-OHB/AcAc ratio than those in normal subjects. The same results were also obtained in **type II** DM patients **treated** by dieting alone whose fasting blood glucose levels were well controlled. The levels of TKB, AcAc, and 3-OHB were higher in **type II** DM patients who were under poor blood glucose control had a high level of free fatty acid and a lowered insulin secretion capacity (.SIGMA..DELTA. CPR120'). The level of TKB, and 3-OHB in diabetics showed a significant positive correlation with **glucagon**: insulin (IRG/CPR) molar ratio. These findings indicate that the levels of fasting serum ketone bodies in diabetics are useful as one of the most important indices for the management of DM.

5/7/55 (Item 55 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005068390 BIOSIS NO.: 198681032281
A COMPARISON OF SERUM C-PEPTIDE RESPONSE TO INTRAVENOUS **GLUCAGON** AND URINE C-PEPTIDE AS INDEXES OF INSULIN DEPENDENCE
AUTHOR: MATSUDA A (Reprint); KAMATA I; IWAMOTO Y; SAKAMOTO Y; KUZUYA T
AUTHOR ADDRESS: DIV ENDOCRINOLOGY AND METABOLISM, JICHI MED SCH, MINAMIKAWACHI-MACHI, TOCHIGI-KEN 329-04, JAPAN**JAPAN
JOURNAL: Diabetes Research and Clinical Practice 1 (3): p161-168
1985
ISSN: 0168-8227
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Serum C-peptide (SCPR) at fasting and after intravenous injection of **glucagon** was evaluated in diabetic patients with various degrees of insulin dependence, and compared with 24 h urine C-peptide (UCPR). Fasting SCPR did not differ between healthy subjects and sulfonylurea-**treated** patients (SU) who were considered to have definite non-insulin dependent **diabetes** (**NIDDM**); but was significantly lower in patients with insulin-dependent **diabetes** (IDDM) (0.24 .+-. 0.10 ng/ml in IDDM vs. 1.43 .+-. 0.61 ng/ml in SU, $P < 0.001$). SCPR reached a peak at 6 min after **glucagon** injection, except for the IDDM group. The SCPR response at 6 min after 1 mg **glucagon** injection was significantly lower in the SU (**NIDDM**) group than in the normal group (2.86 .+-. 1.21 vs. 4.69 .+-. 1.47 ng/ml, $P < 0.001$). In the IDDM group, there was no increase of SCPR after **glucagon** injection. Among diabetic patients, SCPR response to **glucagon** correlated positively to the amounts of UCPR ($P < 0.001$). By analysis of the distribution patterns of SCPR response to intravenous **glucagon**, SCPR of 1.0 ng/ml and the increment of SCPR of 0.5 ng/ml at 6 min are to be used as cut-off points to differentiate IDDM and **NIDDM**. These values correspond roughly to the UCPR values below 20 .mu.g/day and above 30 .mu.g/day, which we previously proposed as indexes to differentiate insulin-dependent and non-insulin-dependent **diabetes**.

5/7/56 (Item 56 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005062775 BIOSIS NO.: 198681026666
COMBINATION OF INSULIN AND GLIBENCLAMIDE IN THE **TREATMENT** OF ELDERLY NON-INSULIN-DEPENDENT **TYPE 2** DIABETIC PATIENTS
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JOURNAL: Annals of Clinical Research 17 (3): p100-104 **1985**
ISSN: 0003-4762
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A double-blind crossover study was undertaken to determine whether glibenclamide could improve glycaemic control in patients not adequately controlled by insulin. Nine elderly outpatients with non-insulin dependent (**type 2**) **diabetes** participated in the study. In addition to their regular insulin **treatment**, the patients were given either glibenclamide 5 mg twice daily or placebo tablets for 2 months followed by the opposite combination for a further 2 months. The fasting plasma glucose concentrations were lower during the insulin plus glibenclamide period than during the insulin plus placebo period and the difference tended to increase at the end of each study period ($p < 0.01$ and 0.001). The level of haemoglobin A (HbA1) decreased significantly from 13.8 .+-. 0.6% (mean .+-. SE) to 12.4 .+-. 0.6% during the insulin+glibenclamide period ($p < 0.01$); in contrast, there was no change during the insulin+placebo period. The 24-hour urinary glucose excretion was reduced during the insulin+glibenclamide period compared with insulin+placebo ($p < 0.05$). Basal and **glucagon** stimulated C-peptide concentrations did not significantly differ between the two **treatment** regimens. The results suggest that glibenclamide can improve the glycaemic control in insulin-**treated** elderly diabetics by mechanisms which still are to be elucidated.

5/7/57 (Item 57 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0005055389 BIOSIS NO.: 198681019280
EFFECT OF CLONIDINE ON GLUCOSE INSULIN AND **GLUCAGON** RESPONSES TO A PROTEIN MEAL IN **TYPE 2** DIABETICS
AUTHOR: FERLITO S (Reprint); INDELICATO G; DI VINCENZO S; DEL CAMPO F; LA VIGNERA A; FICHERA C
AUTHOR ADDRESS: VIA SANTA MADDALENA 47, 95125 CATANIA, ITALY**ITALY
JOURNAL: Journal of Endocrinological Investigation 8 (3): p185-187 **1985**
ISSN: 0391-4097
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The authors investigated the effects of clonidine (.alpha.-2 stimulating agent) on blood glucose, insulin and **glucagon** levels in order to assess the .alpha.-adrenergic regulation of endocrine pancreatic secretion. Ten hypertensive female subjects affected with **type 2 diabetes** were studied; each subject was given a protein

meal (boiled beef 200 g); blood samples were taken at -30, 0, 30, 60, 90 and 120 min; after this test each subject was **treated** for 4 days with clonidine (0.150 mg, 3 times/day per os); at the 5th day the protein meal was repeated under the same conditions except for the added administration of clonidine. Plasma glucose, insulin and **glucagon** were estimated. The administration of a protein meal caused a significant increase of blood glucose (peak at 60 min), insulin (peak at 90 min) and **glucagon** (peak at 90 min) levels; the association of clonidine caused an increase of blood glucose (single values and total areas) without changes of insulin and **glucagon** levels, when compared to those obtained before clonidine **treatment**. In conclusion, the association of clonidine to a protein meal caused impaired glucose tolerance presumably due to a direct glycogenolytic effect, occurring in the liver on account of an .alpha.-2 receptor stimulation, insulin and **glucagon** not being involved in this phenomenon.

5/7/58 (Item 58 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0004798427 BIOSIS NO.: 198580107322
PLASMA C-PEPTIDE RESPONSE DURING **GLUCAGON** TEST AS AN INDEX FOR EVALUATION OF INSULIN REQUIREMENT IN DIABETICS
AUTHOR: SANKE T (Reprint); SATOGAMI E; SOWA R; KURIYAMA S; OKAI K; MORITA H ; SAKAMOTO K; KONDO M; NANJO K; MIYAMURA K
AUTHOR ADDRESS: FIRST DEP MED, WAKAYAMA MED SCH, WAKAYAMA, JAPAN**JAPAN
JOURNAL: Journal of the Japan Diabetes Society 28 (6): p713-719 **1985**
ISSN: 0021-437X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: The significance of .DELTA.CPR5', which represents the difference between the 5 min value of plasma C-peptide (CPR) during **glucagon** test (1 mg i.v.) and the basal value, was investigated in relation to insulin requirement in patients with **diabetes** mellitus (DM). In normal controls, .DELTA.CPR5' (ng/ml) as 4.22 .+-. 0.84 (mean .+-. SE). In 128 outpatients whose plasma glucose levels were stable and well controlled (FBS < 200 mg/dl), .DELTA.CPR5' was 0.23 .+-. 0.08 in type I DM (n = 7); 0.58 .+-. 0.10 in **type II** DM under insulin **treatment** (n = 29); 1.49 .+-. 0.12 in those under **treatment** with sulfonylureas (n = 34); and 1.69 .+-. 0.12 in those on a diet regimen (n = 58). .DELTA.CPR5' was significantly lower in type I and **type II** DM under insulin **treatment** than in those under **treatment** with sulfonylureas and on a diet regimen. .DELTA.CPR5' was below 0.5 in all of the patients with type I DM and below 0.7 in 21 (72%) out of 29 patients with **type II** DM under insulin **treatment**. A sharp decrease in prevalence of insulin-**treated** patients was noted when .DELTA.CPR5' was over 0.8. In DM patients (n = 17) who were hospitalized for insulin **treatment** because of poor control, .DELTA.CPR120' during 50 g-OGTT and 24 h urine CPR excretion at the time of admission failed to distinguish those who were able to become free from insulin **treatment** at a later date (insulin free group) from those who had to continue insulin **treatment** (insulin-continued group), whereas .DELTA.CPR5' during **glucagon** test at the time of admission showed a significant difference (P < 0.001) between both groups: insulin-free group (n = 8) 1.79 .+-. 0.38 and insulin-continued group (n = 9) 0.52 .+-. 0.08. Apparently, .DELTA.CPR5' during **glucagon** test is useful as an index for evaluation of the insulin requirement in diabetics and suggest that less than 0.7 ng/ml .DELTA.CPR5' could be regarded as insulin requirement.

5/7/59 (Item 59 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0004638186 BIOSIS NO.: 198579057085
DIURNAL VARIATIONS OF BLOOD SUGAR IMMUNOREACTIVE INSULIN C-PEPTIDE IMMUNOREACTIVITY AND IODINE-125 INSULIN BINDING CAPACITY IN DIABETICS ON THE BASIS OF DIABETIC TYPE **TREATMENT** STATE OF BLOOD SUGAR CONTROL AND DEGREE OF OBESITY
AUTHOR: MARUMO K (Reprint)
AUTHOR ADDRESS: DEPARTMENT OF MEDICINE III, TOKYO WOMEN'S MEDICAL COLLEGE, JAPAN**JAPAN
JOURNAL: Journal of Tokyo Women's Medical College 54 (8): p665-677 **1984**
ISSN: 0040-9022
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: To investigate the etiology of 'brittle **diabetes**' and the difference between obese and nonobese diabetics, they were classified on the basis of type, **treatment**, state of blood sugar control and degree of obesity, and measured diurnal variations of blood sugar, plasma IRI (immunoreactive insulin), CPR (C-peptide immunoreactivity), 125I-Insulin binding capacity and IRG (immunoreactive **glucagon**). In insulin **treated** diabetics, CPR was remarkably higher in **type II** diabetics and the stable group than in type I diabetics and Labile group. The same tendency was almost recognized about free insulin level, especially elevation of insulin level from pre-breakfast to 2 h after breakfast. It was more remarkable in **type II** diabetics and Stable group than in type I diabetics and Labile group. The opposite tendency about blood sugar level was observed. Insulin antibody highest level was recognized at pre-breakfast. Remarkable reduction occurred after breakfast in **type II** diabetics and stable group (especially in the latter). An inverse correlation occurred between insulin antibody and free insulin level in the stable group. Plasma **glucagon** tendened to increase inappropriately at the hyperglycemic stage after every meal. In non-insulin dependent diabetics (**NIDDM**) and normals higher levels of IRI and CPR were recognized in the obese group than in nonobese group. The IRI:CPR ratio, had a higher value in the nonobese group than in obese group. A lower IRI:CPR ratio was observed in normals than in **NIDDM**. Variations of CPR and free insulin participate exceedingly in the stability of control of blood sugar level. In respect of **NIDDM** (especially nonobese group), it is suggested that there is a decrease of hepatic extraction of insulin as compared with normal subjects.

5/7/60 (Item 60 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0004620716 BIOSIS NO.: 198579039615
STUDIES ON THE RELEASE AND BIOSYNTHESIS OF PANCREATIC HORMONES THE EFFECT OF TRISHYDROXYMETHYLAMINOMETHANE ON RELEASE OF INSULIN **GLUCAGON** AND SOMATOSTATIN AND BIOSYNTHESIS OF INSULIN IN RAT PANCREATIC ISLETS
AUTHOR: EJIRI K (Reprint)
AUTHOR ADDRESS: SECOND DEPARTMENT OF INTERNAL MEDICINE, KOBE UNIVERSITY SCHOOL OF MEDICINE, JAPAN**JAPAN
JOURNAL: Medical Journal of Kobe University 44 (4): p63-76 **1983**

ISSN: 0075-6431
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: The Golgi apparatus and Golgi-endoplasmic reticulum-lysosomal (GERL) system are known to be important subcellular organelles in endocrine cells. In pancreatic .beta. cells these organelles were considered to be the site for the conversion of proinsulin to insulin largely by autoradiographic studies. The Golgi membrane and the GERL system in various cells was recently found to be affected by tris(hydroxymethyl)aminomethane (Tris). No reports were encountered to clarify the relationships of the Golgi area and insulin biosynthesis biochemically using agents to selectively affect the area. The effect of Tris on insulin biosynthesis and release of insulin and the morphology of islets was studied. **Glucagon** and somatostatin release was studied. Rat islets were isolated by the collagenase method and preincubated in Krebs-Henseleit bicarbonate buffer (KHBB, pH 7.4) containing 3.3 mM glucose and 0.5% bovine serum albumin (BSA) at 37.degree. C for 20 min under a gas phase of 95% O2-5% CO2. Islets were incubated for 60 min in KHBB containing 0.5% BSA and glucose (3.3, 8.3 or 16.7 mM) or 3.3 mM glucose plus 20 mM arginine with and without Tris (1 or 10 mM) under the same conditions as in preincubation. Insulin, **glucagon** and somatostatin release in the medium were radioimmunoassayed. Some islets after incubation were subjected to measurement of immunoreactive proinsulin and insulin contents. For studies on insulin biosynthesis, islets were incubated in KHBB containing 3H-leucine and 16.7 mM glucose with and without 10 mM Tris for 120 min. Insulin in the islets was extracted with 75% acid ethanol. The extracts were fractionated into proinsulin and insulin on Bio-gel P-30 with 3 N acetic acid as eluate and the radioactivity of both fractions was counted. Tris suppressed glucose-induced insulin release, whereas it did not affect the **glucagon** or somatostatin release. Arginine-induced insulin release was suppressed by 1 and 10 mM Tris, whereas the **glucagon** and somatostatin release were not by 1 mM Tris. It was suppressed by 10 mM Tris. Islets preincubated by 10 mM Tris for 20 min showed the suppression of insulin release by 8.3 mM glucose and 20 mM arginine. Immunoreactive proinsulin and insulin contents in 10 mM Tris-**treated** islets were significantly higher than those in islets without Tris **treatment**. 3H-Leucine incorporation into the insulin fraction was suppressed by Tris, but the sum of the radioactivity of both proinsulin and insulin fractions were not influenced. The radioactivity ratio of proinsulin and insulin fraction increased in Tris-**treated** islets. Electron-microscopically, the Golgi apparatus and the GERL system of B cells were affected, but those of A cells were not. Tris seems to destroy selectively the Golgi apparatus and the GERL system in the islet .beta. cells and the area may play a role in insulin biosynthesis and secretion in pancreatic .beta. cells, and Tris may become a useful agent to investigate the mechanism of processing of proinsulin to insulin. Tris also may make an experimental diabetic model for hyperproinsulinemia which is observed in the early stage of **type II diabetes**.

0004334726 BIOSIS NO.: 198478070133

THE COMBINATION OF INSULIN AND SULFONYL UREA IN THE **TREATMENT** OF SECONDARY DRUG FAILURE IN PATIENTS WITH **TYPE II DIABETES**

AUTHOR: GROOP L (Reprint); HARNO K; TOLPPANEN E-M
AUTHOR ADDRESS: THIRD AND FOURTH DEP MED, UNIV HELSINKI, HELSINKI**FINLAND
JOURNAL: Acta Endocrinologica 106 (1): p97-101 **1984**
ISSN: 0001-5598
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Thirteen patients (6 females and 7 males) who were secondary failures on oral drug therapy were randomly allocated to either 2 mo. of **treatment** with insulin + glibenclamide or insulin + placebo. Thereafter the **treatment** schedules of the 2 groups were switched over for another 2 mo. The combination of insulin and glibenclamide was more effective in lowering the fasting blood glucose (P = 0.026) and 24 h urine glucose (P = 0.042) than the combination of insulin and placebo. The combination therapy with insulin and glibenclamide revealed higher basal (P = 0.021) and **glucagon**-stimulated C-peptide concentrations (P = 0.037) than therapy with insulin and placebo. However, insulin binding to erythrocytes did not differ between the 2 study periods. The addition of glibenclamide to insulin in **type II** diabetics poorly controlled by oral antidiabetics alone may slightly improve diabetic control. The mechanism of this action is due at least partly to sulfonylurea-induced stimulation of endogenous insulin secretion. The effectiveness of the combination **treatment** during long-term therapy still remains to be proven.

5/7/62 (Item 62 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0004210608 BIOSIS NO.: 198477042519
LONG-TERM STUDIES ON **GLUCAGON** SECRETION IN DIABETIC CHILDREN
AUTHOR: OHDE S (Reprint)
AUTHOR ADDRESS: DEP PEDIATRICS, NIHON UNIV SCH MED**JAPAN
JOURNAL: Nichidai Igaku Zasshi 42 (4): p397-408 **1983**
ISSN: 0029-0424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: In 28 diabetic children, the pancreatic **glucagon** secretion, especially in relation to management of this disease, was studied by a radioimmunoassay using 30K antigen for about 1 yr. No **glucagon** antibodies were found in 20 patients with insulin-dependent **diabetes** mellitus (IDDM). The mean fasting levels of plasma immunoreactive **glucagon** (IRG) in IDMM and noninsulin-dependent **diabetes** mellitus (**NIDDM**) were significantly higher than those in the control group (P < 0.01, 0.05). When the range of fluctuation of plasma IRG levels in IDDM exceeded 100 pg/ml during the **treatment** period (group A), the mean plasma IRG levels were significantly higher (P < 0.01) than those at below 99 pg/ml (group B), and the mean blood glucose levels were also higher in group A than in group B. Sufficient attention should be paid to the management of IDDM in cases showing fluctuations of plasma IRG levels in excess of 100 pg/ml during the **treatment** period.

5/7/63 (Item 63 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0004132445 BIOSIS NO.: 198427047864
PREVALENCE AND INCIDENCE OF **TYPE II DIABETES** IN DENMARK
COMPARED WITH OTHER COUNTRIES
AUTHOR: DAMSGAARD E M (Reprint)
AUTHOR ADDRESS: FREDERICIA HOSPITAL AND UNIVERSITY INSTITUTE OF CLINICAL GENETICS, ODENSE UNIVERSITY HOSPITAL, ODENSE, DENMARK**DENMARK
JOURNAL: Acta Endocrinologica Supplementum 105 (262): p21-26 **1984**
CONFERENCE/MEETING: SYMPOSIUM ON DIABETES MELLITUS TYPE 2, STOCKHOLM, SWEDEN, APR. 14-15, 1983. ACTA ENDOCRINOL SUPPL.
ISSN: 0300-9750
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

5/7/64 (Item 64 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0004047914 BIOSIS NO.: 198426046841
THE EFFECT OF INSULIN **TREATMENT** ON INSULIN SECRETION AND ACTION IN **TYPE II DIABETES**
AUTHOR: GARVEY T (Reprint); GRIFFIN J; REVERS R; OLEFSKY J; KOLTERMAN O
AUTHOR ADDRESS: DEP MED, UNIV COLO HEALTH SCI CENT, DENVER, CO, USA**USA
JOURNAL: Clinical Research 31 (2): p386A **1983**
CONFERENCE/MEETING: 40TH ANNUAL NATIONAL MEETING OF THE AMERICAN FEDERATION FOR CLINICAL RESEARCH, WASHINGTON, D.C., USA, APR. 29-MAY 2, 1983. CLIN RES.
ISSN: 0009-9279
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

5/7/65 (Item 65 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0003818486 BIOSIS NO.: 198375002429
PANCREATIC **GLUCAGON** SECRETION ITS MECHANISM AND CLINICAL SIGNIFICANCE
AUTHOR: TANESE T (Reprint)
AUTHOR ADDRESS: DEP INTERNAL MED, JIEKI UNIV SCH MED
JOURNAL: Tokyo Jikeikai Medical Journal 97 (1): p23-29 **1982**
ISSN: 0375-9172
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: For the purpose of studying abnormality of **glucagon** secretion in diabetics, response of **glucagon** secretion to glucose **administered** orally (oral glucose tolerance test; OGTT) was investigated. In healthy subjects serum **glucagon** (immunoreactive **glucagon**; IRG) levels decreased during OGTT. In insulin dependent **diabetes** mellitus (IDDM, 10 cases) and noninsulin dependent **diabetes** mellitus (**NIDDM**, 30 cases) IRG levels increased (paradoxical rise). Mild diabetics whose fasting plasma glucose (FPG) values were < 119 mg/dl, showed the 2 phase responses of IRG secretion, i.e., first rising and then late lowering. When observing the effect of **treatment** of diabetics (**NIDDM**) for 1-2 mo. on IRG response, the paradoxical rise still remained after **treatment** even though FPG levels decreased to normal range and IRG levels lowered. Insulin was infused **in vivo** into alloxan diabetic rats that were given

glucose orally. Paradoxical rise in IRG observed in these animals was prevented. Thus abnormality of IRG response in **diabetes** will be normalized if insulin is sufficiently supplied. In the 2nd experiment in which human pancreatic .alpha.-cell clones were used to see the dose-response relationship between IRG release and glucose concentration in the incubation medium with or without addition of insulin (20 mU/ml) IRG release was enhanced significantly in the presence of insulin. Under 2.3 mM glucose concentration it was clearly demonstrated that IRG release increased in proportion to insulin doses added to the medium. Even without insulin in the incubation medium 5.1 mM glucose could inhibit totally IRG release from .alpha.-cell clones. The difference in results in the **in vivo** and in vitro experiments might be due to the different experimental system in the present study but it is suggested that in vitro **glucagon** synthesis might be strongly stimulated by insulin and increased **glucagon** secretion induced necessarily.

5/7/66 (Item 66 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0003751158 BIOSIS NO.: 198325010101
MECHANISM OF ACTION OF GLIBENCLAMIDE IN **TYPE 2** NON-INSULIN-DEPENDENT **DIABETES** DURING LONG-TERM **TREATMENT**
AUTHOR: BECK-NIELSEN H (Reprint); LINDSKOV H O; RICHELSEN B; FABER O; BINDER C
AUTHOR ADDRESS: MED DEP III, CTY HOSP AARHUS, DEN**DENMARK
JOURNAL: Diabetologia 23 (2): p153 **1982**
CONFERENCE/MEETING: 18TH ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES, BUDAPEST, HUNGARY, SEPT. 1-4, 1982. DIABETOLOGIA.
ISSN: 0012-186X
DOCUMENT TYPE: Meeting
RECORD TYPE: Citation
LANGUAGE: ENGLISH

5/7/67 (Item 67 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0003625188 BIOSIS NO.: 198274041611
INFLUENCE OF BETA BLOCKING DRUGS ON GLUCOSE METABOLISM IN PATIENTS WITH NON-INSULIN-DEPENDENT **DIABETES** MELLITUS
AUTHOR: GROOP L (Reprint); TOTTERMAN K-J; HARNO K; GORDIN A
AUTHOR ADDRESS: FIRST DEP MED, UNIV HELSINKI, HELSINKI, FINLAND**FINLAND
JOURNAL: Acta Medica Scandinavica 211 (1-2): p7-12 **1982**
ISSN: 0001-6101
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Two .beta.-blocking agents, non-selective propranolol and .beta.1-selective metoprolol, were investigated with respect to their effects on glucose metabolism in 10 hypertensive patients with non-insulin dependent **diabetes** mellitus (**NIDDM**). The patients were **treated** randomly for 2 wk in a double-blind cross-over manner with (a) propranolol, metoprolol and placebo. Propranolol impaired glucose tolerance when compared to placebo. The increase in blood glucose was associated neither with changes in concentrations of serum insulin, plasma **glucagon** of free fatty acid nor with alterations in peripheral insulin sensitivity as measured by 125I-insulin binding to mononuclear leukocytes. Although metoprolol had no effect on blood

glucose, it increased 125I-insulin binding to mononuclear leukocytes. The increase in insulin binding could contribute to blood glucose control during metoprolol **treatment**. In search for reasons for poor metabolic control in **NIDDM**, **treatment** with non-selective .beta.-blockers should be kept in mind.

5/7/68 (Item 68 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0003508534 BIOSIS NO.: 198273012461
THE EFFECT OF **TREATMENT** OF **TYPE 2** INSULIN INDEPENDENT **DIABETES** MELLITUS ON PLASMA CONCENTRATIONS OF PANCREATIC POLY PEPTIDE AND **GLUCAGON**
AUTHOR: BERGER D (Reprint); FLOYD J C JR; PEK S B
AUTHOR ADDRESS: UNIV MICHIGAN, C7009 OUTPATIENT BUILDING, BOX 002, ANN ARBOR, MICHIGAN 48109, USA**USA
JOURNAL: Diabetologia 21 (2): p120-125 **1981**
ISSN: 0012-186X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of the control of **diabetes** with diet and insulin upon plasma levels of human pancreatic polypeptide and **glucagon** was determined in 8 patients with **Type 2** (insulin independent) **diabetes** mellitus. The mean .+-. standard error of the mean fasting plasma glucose was 15.9 .+-. 1.3 mmol/l for 5 days of diet **treatment** and 5.9 .+-. 0.4 mmol/l for the last 5 days of **treatment** with diet plus insulin ($P < 0.0001$); corresponding fasting plasma pancreatic polypeptide levels were 328 .+-. 97 and 247 .+-. 71 pg/ml ($P < 0.05$) and immunoreactive **glucagon** levels were 95 .+-. 11 and 62 .+-. 6 pg/ml ($P < 0.005$). Cooked ground beef was **administered** on the 1st day of diet **treatment** and on the last day of **treatment** with diet plus insulin; mean maximal rise of pancreatic polypeptide, and total and incremental plasma pancreatic polypeptide response areas were significantly lower following **treatment** ($P < 0.01$), as was total area for immunoreactive **glucagon** ($P < 0.05$). Normalization of fasting plasma glucose by short-term **treatment** with diet plus insulin is associated with decreases in basal and stimulated secretory activity of the pancreatic polypeptide cells in insulin independent **diabetes** mellitus.

5/7/69 (Item 69 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0003040139 BIOSIS NO.: 198070071626
AUTO ANTIBODIES TO DUODENAL GASTRIC INHIBITORY PEPTIDE CELLS AND TO SECRETIN CELLS IN PATIENTS WITH CELIAC DISEASE TROPICAL SPRUE AND MATURITY ONSET **DIABETES**
AUTHOR: MIRAKIAN R (Reprint); BOTTAZZO G F; DONIACH D
AUTHOR ADDRESS: DEP IMMUNOL, ARTHUR STANLEY HOUSE, MIDDX HOSP MED SCH, 40-50 TOTTENHAM ST, LONDON W1P 9PG, ENGL, UK**UK
JOURNAL: Clinical and Experimental Immunology 41 (4): p33-42 **1980**
ISSN: 0009-9104
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The presence of autoantibodies detected by immunofluorescence [IFL] to single endocrine cells of human duodenum is described in 3 groups of patients and 2 control groups. Of 173 celiac cases, 4 had GIP [gastric-inhibitory-peptide] cell antibodies, 1 had secretin cell antibodies and 21 reacted with both cell types. Of 12 tropical sprue sera, 4 reacted with the same 2 cells. Among 50 elderly diabetics **treated** with hypoglycemic drugs, 7 sera gave a positive cytoplasmic IFL on duodenal substrate. Four were identified as GIP cells by use of the appropriate hormone antiserum and 3 reactions were against cells distinct from those stained by anti-GIP, -secretin, -somatostatin, -**glucagon** and -gastrin. Additional gut hormone antisera must be tested to identify these APUD cells. Thirty blood donors and 73 sera from autoimmune endocrine patients gave entirely negative results on unfixed cryostat sections of duodenal mucosa. Although impaired GIP and secretin responses were reported in celiac disease and abnormal GIP values were found in **Type II diabetes**, there is as yet no data to correlate these metabolic dificiencies with the presence of endocrine cell antibodies in the serum.

5/7/70 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

02029321 Genuine Article#: JU805 Number of References: 36
Title: ROLE OF FFA-GLUCOSE CYCLE IN GLUCOREGULATION DURING EXERCISE IN TOTAL ABSENCE OF INSULIN
Author(s): YAMATANI K; SHI ZQ; GIACCA A; GUPTA R; FISHER S; LICKLEY HLA; VRANIC M
Corporate Source: UNIV TORONTO,DEPT PHYSIOL,MED SCI BLDG,RM 3358,1 KINGS COLL CIRCLE/TORONTO M5S 1A8/ONTARIO/CANADA/; UNIV TORONTO,DEPT PHYSIOL,MED SCI BLDG,RM 3358,1 KINGS COLL CIRCLE/TORONTO M5S 1A8/ONTARIO/CANADA/; UNIV TORONTO,DEPT SURG/TORONTO M5S 1A8/ONTARIO/CANADA/; UNIV TORONTO,DEPT MED/TORONTO M5S 1A8/ONTARIO/CANADA/; WOMENS COLL HOSP/TORONTO M5S 1A8/ONTARIO/CANADA/
Journal: AMERICAN JOURNAL OF PHYSIOLOGY, **1992**, V263, N4 (OCT), P E646-E653
ISSN: 0002-9513
Language: ENGLISH Document Type: ARTICLE
Abstract: Muscle contraction in vitro increases glucose uptake (GU), independent of insulin, but **in vivo**, the exercise-induced increase in GU is impaired in insulin-deficient diabetic dogs. We wished to determine whether, **in vivo**, suppression of the free fatty acid (FFA)-glucose cycle with methylpalmoxirate (MP, inhibitor of FFA oxidation) alone or combined with propranolol (PRO, beta-blocker) could improve GU during exercise in the absence of insulin. We performed four groups of exercise experiments (6 km/h, 10% slope) in depancreatized insulin-deprived dogs: 1) control (n = 6); 2) MP **treated** (5 oral doses of 10 mg/kg, twice daily, n = 6); 3) **treated** with MP + octanoate (OCT; oxidation unaffected by MP, 27 mumol.kg-1.min-1 iv during exercise; n = 5); and 4) MP + PRO **treated** (5 mug.kg-1.min-1 iv during exercise, n = 6). MP abolished ketosis (inhibition of hepatic FFA oxidation), decreased basal glucose production (GP), and increased metabolic clearance of glucose (MCR). During exercise, MP attenuated the increment in GP ($P < 0.01$), which was reversed by OCT. MP did not affect the exercise-induced increase in GU and MCR. With MP + PRO, FFAs decreased and lactate did not rise during exercise. GP was not further suppressed, but GU and MCR were increased ($P < 0.01$) to 89 and 31% of normal, respectively. In insulin-deprived depancreatized dogs, glucose cycling was increased to a greater extent than GP, as in **type II diabetes**. By the end of exercise, glucose cycling

increased ($P < 0.05$), but to a similar extent as GP. In conclusion, in the absence of insulin, 1) at rest, inhibition of FFA oxidation with MP inhibits GP and increases MCR; 2) during exercise, inhibition of FFA oxidation blunts GP, but only combined inhibition of FFA oxidation, lipolysis, and perhaps also of muscle glycogenolysis with MP + PRO increases GU and MCR; and 3) because MP + PRO can improve GU and MCR in depancreatized dogs, an important action of insulin on the exercise-induced glucose uptake may be indirect through restraint of lipolysis and muscle glycogenolysis.

5/7/71 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01901128 Genuine Article#: JK179 Number of References: 187
Title: GLUCOSE-TURNOVER - A KEY TO UNDERSTANDING THE PATHOGENESIS OF **DIABETES** (INDIRECT EFFECTS OF INSULIN)
Author(s): VRANIC M
Corporate Source: UNIV TORONTO,FAC MED,DEPT PHYSIOL,MED SCI BLDG,1 KINGS COLL CIRCLE/TORONTO M5S 1A8/ONTARIO/CANADA/; UNIV TORONTO,FAC MED,DEPT MED/TORONTO M5S 1A8/ONTARIO/CANADA/
Journal: DIABETES, **1992**, V41, N9 (SEP), P1188-1206
ISSN: 0012-1797
Language: ENGLISH Document Type: REVIEW
Abstract: This article is divided into two parts. A retrospective overview summarizes some of the work that provided the framework and tools of the more recent studies. The five novel areas of research are related to the indirect effects of insulin. Regulation of plasma glucose is of central importance in health and **diabetes**. Understanding this precise regulation requires sensitive isotope dilution methods that can measure the rates at which glucose is produced by the liver and used by the tissues on a minute-to-minute basis. Validation studies indicated that the non-steady-state tracer method yields reasonable results when the specific activity of plasma glucose does not change abruptly. During hyperinsulinemic glucose clamps, the decrease in specific activity of glucose can be prevented by the MSTI. During exercise, the decrease of specific activity can be only in part ameliorated by step-tracer infusion. Depancreatized dogs are used extensively as a model of selective insulin deficiency, because dog stomach secretes physiological amounts of **glucagon**. This strategy can avoid injections of somatostatin, which can have other affects in addition to the suppression of insulin and **glucagon**. In human **diabetes**, in addition to an increase of glucose production, there is also an increase in glucose cycling in the liver. In animal models of **diabetes**, mild **NIDDM**, and in glucose intolerance, the percentage of increments of glucose cycling are much larger than those of glucose production. We hypothesize, therefore, that measurements of glucose cycling can be used as an early marker of glucose intolerance. Application of different tracer strategies and use of the depancreatized dog as a model of **diabetes**, we investigated the importance of the indirect effects of insulin in the pathogenesis of **diabetes**. 1) Because, in the **treatment** of IDDM, insulin is **administered** by the peripheral routes we compared the relative importance of hepatic and peripheral effects of insulin in regulating the rate of glucose production. Experiments were performed in depancreatized dogs that were initially maintained at moderate hyperglycemia (10 mM) with subbasal portal insulin infusion. During the experimental period, insulin was infused either peripherally or portally at 0.9 mU . kg-1 . min-1. In addition, peripheral infusions were also given at 0.45 mU . kg-1 . min-1. We concluded that when suprabasal insulin levels are provided to moderately hyperglycemic

depancreatized dogs, the suppression of glucose production is more dependent on peripheral than portal insulin concentrations. This indirect effect of insulin may be mediated by limitation of the flow of precursors and energy substrates for gluconeogenesis and/or by suppressive effect of insulin on **glucagon** secretion. These results suggest that the absence of a portal-peripheral gradient in insulin-**treated** diabetic subjects may not be important for postprandial suppression of glucose production. 2) The **glucagon** -insulin ratio is an important regulator of glucose production by the liver during moderate exercise, whereas during intense exercise the catecholamines play a prominent role. Regulation of glucose uptake during exercise is very complex. **In vivo**, insulin can play an indirect role by inhibiting the FFA-glucose cycle and by maintaining normoglycemia; both of these factors influence glucose uptake by the muscle.

3) Streptozocin-induced **diabetes** in rats decreases the number of glucose transporters when measured both by cytochalasin B binding and by assessment of GLUT4 transporters. Normalization of glycemia in the diabetic rats by a 2-day phlorizin **treatment**, which does not affect the insulin concentration, normalizes glucose transporter number in the plasma membrane. We concluded that hyperglycemia, per se, plays an important role in regulating glucose transporter number in the muscle. 4) In alloxan-induced diabetic dogs, similarly to IDDM, **glucagon**'s response and, therefore, the response of glucose production to declining glucose is impaired. We present a new hypothesis that an increased ratio between somatostatin and **glucagon** in the residual diabetic islets of diabetic dogs can, at least in part, explain the lack of **glucagon** response to hypoglycemia. 5) To investigate the effect of stress in diabetic animals, we used an intracerebroventricular injection of a small amount of carbachol. This compound increases the release of all counterregulatory hormones, but without affecting insulin secretion. Surprisingly, this release of counterregulatory hormones induces only a marginal change in plasma glucose, because increased glucose production is matched by a similar increase in glucose uptake. In contrast, in hyperglycemic diabetic dogs, the same carbachol injection induces a sevenfold larger increment in plasma glucose. This occurred because the metabolic clearance rate of glucose does not increase. We therefore postulated a neural mechanism that controls peripheral glucose uptake and does not require a regulatory effect of insulin. A permissive role of insulin could be to maintain normal insulin sensitivity in the muscle. From the point of view of the clinician, if diabetic neuropathy affects this pathway, this would contribute to insulin resistance. However, even more important is the possibility that this pathway may take part in the pathogenesis of **diabetes**.

5/7/72 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01832942 Genuine Article#: JE403 Number of References: 45
Title: C-PEPTIDE PROFILES IN PATIENTS WITH NON-INSULIN-DEPENDENT **DIABETES**-MELLITUS BEFORE AND DURING INSULIN-**TREATMENT**
Author(s): LINDSTROM T; ARNQVIST HJ; LUDVIGSSON J; VONSCHENCK HH
Corporate Source: LINKOPING UNIV HOSP,DEPT INTERNAL MED/S-58185 LINKOPING//SWEDEN/; LINKOPING UNIV HOSP,DEPT PEDIAT/S-58185 LINKOPING//SWEDEN/; LINKOPING UNIV HOSP,DEPT CLIN CHEM/S-58185 LINKOPING//SWEDEN/
Journal: ACTA ENDOCRINOLOGICA, **1992**, V126, N6 (JUN), P477-483
Language: ENGLISH Document Type: ARTICLE

Abstract: The objective of the study was to evaluate the effect of insulin **treatment** on insulin secretion in patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**). Ten patients with **NIDDM** were first investigated while still taking oral hypoglycemic agents, and then randomized to a crossover study with two eight-week periods of insulin **treatment** (oral **treatment** having been stopped) given either as mainly intermediate-acting insulin twice daily (2-dose) or as preprandial regular insulin and intermediate-acting insulin at bedtime (4-dose). In the patients **treated** with oral agents the 24-h C-peptide area under the curve was similar to that in the controls, but the profile was different with a rise at breakfast but with almost absent meal peaks during the rest of the day. Insulin **treatment** improved glycemic control markedly, lowered urinary C-peptide excretion and the serum C-peptide concentrations being reduced by more than 50%. The shape of the C-peptide profiles was unaltered and there were no significant differences between the two insulin regimens. The decrease in serum C-peptide concentration during insulin **treatment** correlated with the change in blood glucose. Fasting serum C-peptide concentrations correlated closely with the 24-h C-peptide area under the curve. In conclusion, insulin **treatment** of **NIDDM** patients with secondary failure to oral agents greatly reduces the insulin secretion, probably owing to the reduction in blood glucose.

5/7/73 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01606363 Genuine Article#: HL175 Number of References: 16
Title: DEXAMETHASONE **TREATMENT** FAILS TO INCREASE ARGININE-INDUCED INSULIN RELEASE IN HEALTHY-SUBJECTS WITH LOW INSULIN-RESPONSE
Author(s): GRILL V; ALVARSSON M; EFENDIC S
Corporate Source: KAROLINSKA HOSP,DEPT ENDOCRINOL/S-10401 STOCKHOLM 60//SWEDEN/
Journal: DIABETOLOGIA, **1992**, V35, N4 (APR), P367-371
Language: ENGLISH Document Type: ARTICLE
Abstract: We have compared insulin responses to L-arginine before and during dexamethasone **treatment** in healthy subjects, previously classified as subjects with either high or low insulin response according to a standardized glucose infusion test. Arginine stimulation was **administered** as a 150 mg/kg bolus followed by 10 mg.kg-1.min-1 to six subjects with high insulin response and to seven subjects with low insulin response. Before dexamethasone **treatment** the incremental insulin level during 0-10 min of arginine was higher in subjects with high (36.5 +/- 6.8-mu-U/ml) than in subjects with low response (14.5 +/- 2.3-mu-U/ml), $p < 0.01$ for difference. Dexamethasone **treatment** (6 mg/day for 60 h) markedly enhanced the insulin response to arginine in subjects with high response (+ 99% 0-30 min) but failed to affect the subjects with low response (+ 4% 0-30 min). The C-peptide response to arginine exhibited similar differences between groups. Decreased responsiveness to arginine in subjects with low insulin response, especially during dexamethasone **treatment**, suggests a Beta-cell capacity defect although a decreased potentiating-sensing effect of glucose cannot be completely ruled out.

5/7/74 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01552247 Genuine Article#: HH179 Number of References: 30
Title: NORMOGLYCEMIA PER SE BUT NOT NORMOINSULINEMIA IS RESPONSIBLE FOR SUPPRESSING ENDOGENOUS INSULIN-SECRETION AFTER ORAL GLUCOSE-LOAD IN **NIDDM**
Author(s): YAMASAKI Y; KAWAMORI R; BANDO K; KATSURA M; IWAMA N; KUBOTA M; SHICHIRI M; KAMADA T
Corporate Source: OSAKA UNIV,SCH MED,DEPT MED 1,1-1-50 FUKUSHIMA,FUKUSHIMA KU/OSAKA 553//JAPAN/
Journal: DIABETES RESEARCH AND CLINICAL PRACTICE, **1992**, V15, N2 (FEB) , P113-119
Language: ENGLISH Document Type: ARTICLE
Abstract: It is well known that intensive insulin **treatment** of non-insulin-dependent diabetics (**NIDDM**) suppresses endogenous insulin secretion and thereafter improves it. To determine whether 'peripheral normoinsulinemia' or 'normoglycemia' established by the **treatment** is responsible for this suppression, the following five experiments were conducted on 15 well-controlled non-obese **NIDDM** patients. Experiment 1: a 100 g oral glucose load (OGL) was performed and blood glucose was monitored by an artificial endocrine pancreas (AP). Experiment 2: a 100 g OGL was done and blood glucose was normalized by AP-controlled insulin infusion. Experiments 3 and 4: a 100 g OGL was conducted while 'hyperglycemia' seen in experiment 1 was mimicked by AP-controlled glucose infusion with pre-programmed insulin infusion at the same rates as those in experiment 2 ('normoinsulinemia') or at rates 1.5 times higher than those in experiment 2 ('relative hyperinsulinemia'), respectively. Experiment 5: a 40 g OGL was conducted while AP-controlled insulin and glucose infusions were **administered** to make the plasma insulin level lower than in experiment 2 ('hypoinsulinemia') and to mimic the normoglycemic profile observed in experiment 2, respectively. In experiments 3 and 4, neither 'normoinsulinemia' nor 'relative hyperinsulinemia' suppressed the increase in plasma C-peptide after a 100 g OGL. In experiment 5, where the plasma insulin level showed a significantly ($P < 0.05$) lower level than in experiment 2 and glycemia was normalized, C-peptide did not show a significant rise after OGL. These results indicate that 'normoglycemia' rather than 'normoinsulinemia' attained during exogenous insulin therapy, is responsible for suppressing endogenous insulin secretion against orally **administered** glucose.

5/7/75 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01463370 Genuine Article#: HA606 Number of References: 16
Title: PLASMA ISLET AMYLOID POLYPEPTIDE LEVELS IN OBESITY, IMPAIRED GLUCOSE-TOLERANCE AND NON-INSULIN-DEPENDENT **DIABETES**-MELLITUS
Author(s): ENOKI S; MITSUKAWA T; TAKEMURA J; NAKAZATO M; ABURAYA J; TOSHIMORI H; MATSUKARA S
Corporate Source: MIYAZAKI MED COLL,DEPT INTERNAL MED 3,5200 KIHARA/MIYAZAKI 88916//JAPAN/
Journal: DIABETES RESEARCH AND CLINICAL PRACTICE, **1992**, V15, N1 (JAN) , P97-102
Language: ENGLISH Document Type: ARTICLE
Abstract: We examined the response of plasma islet amyloid polypeptide (IAPP) to an oral glucose load in non-obese and obese subjects with normal glucose tolerance or impaired glucose tolerance (IGT), and in non-obese patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**). Plasma IAPP response to intravenous **glucagon** injection in **NIDDM** patients was also studied. Plasma IAPP concentration was determined by a sensitive and specific

radioimmunoassay. Basal levels of plasma IAPP in non-obese subjects with normal glucose tolerance, IGT and **NIDDM** were not significantly different from each other. Non-obese subjects with IGT showed delayed and higher plasma IAPP response to oral glucose load compared to normal non-obese subjects. In **NIDDM** patients, IAPP response to glucose was delayed and lower when compared to normal non-obese subjects. Basal levels of plasma IAPP in normal obese subjects and obese subjects with IGT were significantly higher than those in normal non-obese subjects. Plasma IAPP response to glucose load in these obese subjects was higher than that in normal non-obese subjects. Plasma IAPP response was decreased in diabetic patients **treated** with diet, oral hypoglycemic agents and insulin in that order. We conclude that the secretion of IAPP is reduced with progression of **NIDDM**, although it appears to be rather augmented in IGT compared to normal non-obese subjects.

5/7/76 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01408444 Genuine Article#: GW888 Number of References: 23
Title: VARIATION OF ENDOGENOUS INSULIN-SECRETION IN ASSOCIATION WITH **TREATMENT** STATUS - ASSESSMENT BY SERUM C-PEPTIDE AND MODIFIED URINARY C-PEPTIDE
Author(s): AOKI Y
Corporate Source: SHINSHU UNIV,SCH MED,DEPT INTERNAL MED 2,3-1-1 ASAHI/MATSUMOTO/NAGANO 390/JAPAN/
Journal: DIABETES RESEARCH AND CLINICAL PRACTICE, **1991**, V14, N3 (DEC) , P165-173
Language: ENGLISH Document Type: ARTICLE
Abstract: The variation of endogenous insulin secretion in association with fasting plasma glucose (FPG) level and the modality of **treatment** was assessed using serum C-peptide levels before and after breakfast and the corrected value of 24-h urinary C-peptide (24 h-UCP) in inpatients with non-insulin-dependent **diabetes** mellitus. The corrected value calculated as 24 h-UCP/(urinary C-peptide to creatinine clearance (CCP/CCR) ratio in the fasting state x 10) was correlated with the sum of day-long serum C-peptide levels (r = 0.93) more closely than the measured value of 24 h-UCP (r = 0.79) in 9 patients. In 52 patients **treated** with diet alone, 38 with sulfonylurea and 28 with insulin, fasting serum C-peptide level did not vary with FPG level, and the increment of serum C-peptide level after breakfast and the correlated value of 24 h-UCP decreased with the rise in FPG level in each **treatment**. These indexes were the lowest in insulin **treatment** among the patients with similar FPG levels. In conclusion, 24 h-UCP was demonstrated to be able to reflect day-long endogenous insulin secretion more faithfully after the correction with the CCP/CCR ratio. It was estimated that the insulin response to breakfast and day-long insulin secretion decreased with the rise in FPG level, but basal insulin secretion was maintained over a wide range of FPG levels in each **treatment**. Endogenous insulin secretion seemed to be somewhat suppressed or rested by exogenous insulin in insulin-**treated** patients.

5/7/77 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01344240 Genuine Article#: GQ607 Number of References: 12
Title: RESTORATION OF SENSITIVITY TO SULFONYLUREA AFTER STRICT GLYCEMIC

CONTROL WITH INSULIN IN NONOBESE **TYPE-2** DIABETIC SUBJECTS
Author(s): TORELLA R; SALVATORE T; COZZOLINO D; GIUNTA R; QUATRARO A; GIUGLIANO D
Corporate Source: POLICLIN UNIV NAPOLI 1,1ST MED GEN,PIAZZA L MIRAGLIA/I-80138 NAPLES//ITALY/; NAPLES UNIV,FAC MED 1,CHAIR GERIATR PATHOL/I-80138 NAPLES//ITALY/; NAPLES UNIV,FAC MED 1,CHAIR DIABETOL/I-80138 NAPLES//ITALY/
Journal: DIABETE & METABOLISME, **1991**, V17, N5, P443-447
Language: ENGLISH Document Type: ARTICLE
Abstract: Ten non-obese **type 2** diabetic patients with secondary failure to sulfonylureas received an intensive insulin therapy (four doses schedule) for 90 days. The glycaemic control was poor at entry (HbA1c = 11.7 +/- 1.2 %) and ameliorated significantly after insulin (HbA1c = 7.1 +/ 0. 7 %, p < 0.01). The reintroduction of the sulfonylurea after insulin withdrawal resulted in a persistent satisfactory long-term control (300 days) in all, but two diabetics responded no more after about 3 and 4 months of clinical remission (good control on sulfonylurea). Both basal and stimulated (iv **glucagon** and mixed meal) beta-cell secretory activity increased significantly at 3 months and declined thereafter without falling below baseline values. Three months of strict metabolic control seem to restore the sensitivity to sulfonylurea by enhancing beta-cell secretory activity in non-obese **type 2** diabetic patients.

5/7/78 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01324993 Genuine Article#: GP167 Number of References: 26
Title: INFLUENCE OF SHORT-TERM VERAPAMIL **TREATMENT** ON GLUCOSE-METABOLISM IN PATIENTS WITH NON-INSULIN-DEPENDENT **DIABETES**-MELLITUS
Author(s): SORENSEN MB; SJOSTRAND H; SENGELOV H; THRANE MT; HOLST JJ; LYNGSOE J
Corporate Source: BISPEBJERG HOSP,DEPT MED C/DK-2400 COPENHAGEN//DENMARK/; BISPEBJERG HOSP,DEPT MED C/DK-2400 COPENHAGEN//DENMARK/; UNIV COPENHAGEN,PANUM INST,INST MED PHYSIOL C/DK-2200 COPENHAGEN//DENMARK/
Journal: EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY, **1991**, V41, N5, P 401-404
Language: ENGLISH Document Type: ARTICLE
Abstract: The effect of a sustained-release verapamil preparation on glucose metabolism was investigated in 10 patients with non-insulin dependent **diabetes** mellitus.

In a single blind cross-over study verapamil 240 mg b.d. for 1 week lowered fasting plasma glucose from a mean value of 11.6 mmol/l to 10.3 mmol.l-1, and the fasting glucose appearance rate was decreased from 1.5 to 1.2 mmol.min-1. The decrease in fasting plasma glucose and glucose appearance rate was not related to the steady state plasma concentration of verapamil, nor-verapamil and the metabolites D.617 and D.620.

After oral glucose administration a tendency to lower plasma glucose values was found after verapamil administration. Plasma insulin, C-peptide, total and C-terminal **glucagon** were not significantly different in the placebo and the verapamil studies, neither in the fasting state nor after glucose.

It is concluded that brief verapamil **treatment** decreases fasting plasma glucose and glucose turn-over in non-insulin dependent diabetics, possibly by inhibition of gluconeogenesis.

5/7/79 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01219279 Genuine Article#: GF195 Number of References: 37
Title: BETA-CELL DYSFUNCTION IN HYPERGLYCEMIC RAT MODELS - RECOVERY OF GLUCOSE-INDUCED INSULIN-SECRETION WITH LOWERING OF THE AMBIENT GLUCOSE LEVEL
Author(s): LEAHY JL; WEIR GC
Corporate Source: JOSLIN DIABET CTR,DIV RES,1 JOSLIN PL/BOSTON//MA/02215; BRIGHAM & WOMENS HOSP,DEPT MED/BOSTON//MA/02115; HARVARD UNIV,NEW ENGLAND DEACONESS HOSP,SCH MED,DEPT MED/BOSTON//MA/02215
Journal: DIABETOLOGIA, **1991**, V34, N9, P640-647
Language: ENGLISH Document Type: ARTICLE
Abstract: Glucose-induced insulin secretion is lost in the face of chronic hyperglycaemia. The same defect is present when normal rats are made hyperglycaemic by 48-h glucose infusions. Insulin secretory responses were mapped out during the post-infusion period in order to determine how long it takes for normal Beta-cell function to recover, and to identify factors which influence the rate of recovery. Male Sprague Dawley rats weighing 200-250 g were infused with 50% glucose or 77 mmol/l NaCl for 48 h. The glucose-infused rats were mildly hypoglycaemic for 14 h after the infusion ceased. Glucose-induced insulin secretion, absent at the end of the glucose infusion, was normal 6 h post-infusion. Such rapid recovery was not because of the short duration of hyperglycaemia; mild hypoglycaemia from a 5-h insulin infusion in 90% pancreatectomized rats resulted in a four-fold rise in glucose-induced insulin secretion. Under in vitro conditions, extreme glucose deprivation caused by perfusing the pancreas of glucose-infused rats with buffer devoid of glucose restored glucose-induced insulin secretion in just 37 min. Therefore, the suppression of glucose-induced insulin release by chronic hyperglycaemia is a dynamic situation that requires ongoing hyperglycaemia to prevent the reappearance of glucose responsiveness. This study shows recovery of glucose-induced insulin secretion after just 6 h of mild hypoglycaemia **in vivo** and even faster recovery with more severe glucose deprivation in vitro. Our results suggest that there is an inverse relationship between the rate of return of Beta-cell glucose responsiveness and the ambient glucose concentration.

5/7/80 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01188007 Genuine Article#: GC854 Number of References: 0
(NO REFS KEYED)
Title: EARLY MORNING HYPERGLYCEMIA DAWN PHENOMENON IN NON-INSULIN-DEPENDENT **DIABETES**-MELLITUS (**NIDDM**) - EFFECTS OF CORTISOL SUPPRESSION BY METYRAPONE
Author(s): ATIEA JA; ASLAN SMA; OWENS DR; LUZIO S
Corporate Source: UNIV WALES COLL MED,DEPT MED,DIABET RES UNIT,HEATH PK/CARDIFF CF4 4XN/S GLAM/WALES/; UNIV WALES COLL MED,DEPT MED,DIABET RES UNIT,HEATH PK/CARDIFF CF4 4XN/S GLAM/WALES/
Journal: DIABETES RESEARCH CLINICAL AND EXPERIMENTAL, **1990**, V14, N4
, P181-185
Language: ENGLISH Document Type: ARTICLE
Abstract: To assess the effect of metyrapone on the early morning plasma glucose (PG) rise, seven **NIDDM** patients were studied from 2400 to 0900 h on two separate occasions one week apart.

During the control study nights, patients received conventional therapy only (diet plus sulphonylurea) whereas on **treatment** nights, patients received in addition 30 mg/kg metyrapone orally at 2400 h. The plasma glucose (PG) levels from 0530 to 0900 h were significantly higher during the control night than the corresponding values following metyrapone. The control mean PG concentrations increased continuously from a nadir 8.4 +/- 1.1 mmol/l at 0400 h to a maximum of 9.4 +/- 1.1 mmol/l at 0800 h ($p < 0.01$). In contrast following metyrapone administration a continuous decline in the PG concentration was noted from 2400 to 0800 h. The plasma glucose levels fell from 9.0 +/- 1.2 at 0400 h to 7.7 +/- 1.0 mmol/l at 0800 h ($p < 0.05$). The mean overnight cortisol levels were 167.2 +/- 13.2 and 55.9 +/- 6.4 nmol/l ($p < 0.001$) during the control and **treatment** studies, respectively. The cortisol levels were significantly higher during the control study at all time points from 0400 to 0900 h. No significant changes in insulin, C-peptide, **glucagon**, GH or catecholamine levels were observed between the two study periods. We conclude that the physiologic early morning rise in plasma cortisol possibly contributes to the pathogenesis of the dawn phenomenon in **NIDDM** patients.

5/7/81 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01095374 Genuine Article#: FV982 Number of References: 26
Title: COMPARISON OF BETA-CELL FUNCTION AFTER LONG-TERM **TREATMENT** WITH EITHER INSULIN, INSULIN PLUS GLICLAZIDE OR GLICLAZIDE IN NEONATAL STREPTOZOTOCIN-INDUCED NON-INSULIN-DEPENDENT DIABETIC RATS
Author(s): KAWAI K; SUZUKI S; MURAYAMA Y; WATANABE Y; YAMASHITA K
Corporate Source: UNIV TSUKUBA,INST CLIN MED,DEPT INTERNAL MED/SAKURA/IBARAKI 305/JAPAN/
Journal: DIABETES RESEARCH AND CLINICAL PRACTICE, **1991**, V12, N3, P 163-172
Language: ENGLISH Document Type: ARTICLE
Abstract: There are no definite guidelines in the **treatment** of non-insulin-dependent **diabetes** mellitus (**NIDDM**) as to whether the **treatment** of choice is insulin, a sulfonylurea or a combination of insulin and sulfonylurea. We have therefore tried to evaluate the long-term effects of these **treatments** on beta-cell function in a rat model of **NIDDM**. **NIDDM** rats were prepared by the injection of streptozotocin (60 mg, i.p.) on the 5th day after birth. At 10 weeks, an oral glucose tolerance test (2 g/kg) was performed and rats were divided into 4 groups, each of which had the same mean glucose tolerance. The **treatment** of each group with either NPH insulin (4 U/kg/day), or oral gliclazide (10 mg/kg/day by a stomach cannula), or a combination of the above two, or a control (vehicle for gliclazide) was started from 12 weeks of age and continued for 6 months. Rats were fed ad libitum with standard rat chow. The weight gain of diabetic rats **treated** with gliclazide alone and of the vehicle-**treated** diabetic rats during 6 months was less than that of the other groups receiving insulin. The fasting plasma glucose of the insulin-only **treated** group stayed at the initial level for 6 months, but that of the other groups increased gradually. The frequency of deterioration of glucose tolerance for oral glucose loading (2 g/kg) in the insulin-only **treated** group was smaller than that in the other diabetic groups at 3 at 6 months after the start of **treatment**. The increase in plasma IRI after the oral glucose loading of the insulin-only **treated** group was the largest among the 4 groups at 6 months. In the pancreas perfusion experiment, the

insulin response to glucose in the insulin-only **treated** group was more preserved than that in the other groups of diabetic rats after 6 months of **treatment**. These results suggest that **treatment** with insulin is effective in preserving beta-cell function in a rat model of **NIDDM**, whereas **treatment** with a sulfonylurea agent is not only ineffective but might negate the protective effect of insulin because the insulin-plus-gliclazide **treated** group elicited results similar to those of the gliclazide-only **treated** group except for the weight gain.

5/7/82 (Item 13 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

00833828 Genuine Article#: FA072 Number of References: 0
(NO REFS KEYED)
Title: TWICE DAILY INSULIN THERAPY IN PATIENTS WITH **TYPE-2 DIABETES** AND SECONDARY FAILURE TO SULFONYLUREAS
Author(s): WOLFFENBUTTEL BHR; WEBER RFA; WEEKS L; VANKOETSVELD PM; VERSCHOOR L
Corporate Source: STATE UNIV LIMBURG HOSP,DEPT INTERNAL MED,DIV ENDOCRINOL,POB 1918/6201 BX MAASTRICHT//NETHERLANDS/
Journal: DIABETES RESEARCH CLINICAL AND EXPERIMENTAL, **1990**, V13, N2 , P79-84
Language: ENGLISH Document Type: ARTICLE
Abstract: In 26 **type 2** diabetic patients with failure to diet and sulphonylureas (fasting blood glucose levels > 8.0 mmol/l) the effects of insulin therapy on blood glucose control, islet B-cell function and plasma lipids were studied. Age was 58 +/- 11 (SD) yr, median duration of **diabetes** 6.5, range 1-24 yr, and body mass index 24.5, range 18.9-36.3 kg/m2. Six patients were obese. Therapy comprised twice daily injections of intermediate-acting insulin with additional fast-acting insulin when necessary. After six months, insulin dose was 39 +/- 10 U in the non-obese patients. Their fasting (14.0 +/- 2.7 mmol/l) and post-prandial blood glucose (17.9 +/- 4.5 mmol/l) and glycosylated haemoglobin (HbA1, 13.0 +/- 2.0%) declined to 7.7 +/- 1.6 mmol/l, 10.6 +/- 2.6 mmol/l and 9.5 +/- 1.0%, respectively ($p < 0.001$). Median body weight increased by 3.7 kg ($p < 0.001$). The changes in body weight correlated well with the changes in fasting blood glucose ($r = -0.75$, $p < 0.01$) and HbA1 ($r = -0.73$, $p < 0.01$). Fasting plasma insulin increased ($p < 0.01$), whereas fasting plasma C-peptide and C-peptide release after **glucagon** did not change. Free fatty acids, LDL-cholesterol, total and VLDL-triglycerides showed a significant ($p < 0.05$) decrease during insulin **treatment**. In the six obese patients insulin dose after six months was 44 +/- 18 U. Fasting blood glucose fell from 11.3 +/- 2.2 to 8.8 +/- 2.7 mmol/l ($p < 0.01$), and HbA1 decreased from 10.7 +/- 1.1% to 9.8 +/- 1.3% ($p < 0.01$). Body weight remained unchanged. Fasting C-peptide levels decreased ($p < 0.01$), whereas neither insulin levels nor lipid parameters showed significant changes. Almost all patients reported improved well-being. One patient had a hypoglycaemic period, requiring medical assistance. We conclude that insulin therapy in **type 2** diabetic patients failing on sulphonylurea therapy improved metabolic control with a slight improvement of lipid profile, despite a concomitant gain of weight.

5/7/83 (Item 14 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

00831456 Genuine Article#: FA035 Number of References: 58
Title: ACE-INHIBITION INCREASES HEPATIC AND EXTRAHEPATIC SENSITIVITY TO INSULIN IN PATIENTS WITH **TYPE-2** (NON-INSULIN-DEPENDENT) **DIABETES**-MELLITUS AND ARTERIAL-HYPERTENSION
Author(s): TORLONE E; RAMBOTTI AM; PERRIELLO G; BOTTA G; SANTEUSANIO F; BRUNETTI P; BOLLI GB
Corporate Source: UNIV PERUGIA,IST PATOL MED,VIA E DAL POZZO/I-06100 PERUGIA//ITALY/; UNIV PERUGIA,IST PATOL SPECIALE MED/I-06100 PERUGIA//ITALY/; UNIV PERUGIA,METODOL CLIN/I-06100 PERUGIA//ITALY/
Journal: DIABETOLOGIA, **1991**, V34, N2, P119-125
Language: ENGLISH Document Type: ARTICLE
Abstract: To assess the effects of ACE-inhibition on insulin action in **Type 2** (non-insulin-dependent) **diabetes** mellitus associated with essential hypertension, 12 patients with **Type 2 diabetes** (on diet and oral hypoglycaemic agents) and arterial hypertension were examined on two occasions, in a single blind, cross-over study, after two days of **treatment** with either captopril or a placebo. The study consisted of a euglycaemic-hyperinsulinaemic clamp (two sequential steps of insulin infusion at the rates of 0.25 mU.kg-1.min-1 and 1 mU.kg-1.min-1, 2 h each step), combined with an infusion of 3-H-3-glucose to measure the rate of hepatic glucose production and that of peripheral glucose utilization. The results show that blood pressure was lower after captopril (sitting, systolic 148 +/- 5 mm Hg, diastolic 89 +/- 2 mm Hg) compared to placebo (155 +/- 6 and 94 +/- 2 mm Hg) ($p < 0.05$). Captopril **treatment** resulted in a more suppressed hepatic glucose production (2.7 +/- 0.4 vs 4.94 +/- 0.55-mu-mol.kg-1.min-1), and a lower plasma non-esterified fatty acid concentration (0.143 +/- 0.05 vs 0.200 +/- 0.05 mmol/l) (captopril vs placebo, $p < 0.05$) at the end of the first step of insulin infusion (estimated portal plasma insulin concentration 305 +/- 28 pmol/l); and in a greater glucose utilization (36.5 +/- 5.1 vs 28 +/- 3.6-mu-mol.kg-1.min-1, $p < 0.001$) at the end of the second step of insulin infusion (arterial plasma insulin concentration of 604 +/- 33 pmol/l). We conclude that captopril improved insulin sensitivity in **Type 2 diabetes** associated with hypertension at the level of the liver and extrahepatic tissues, primarily muscle and adipose tissue. Thus, in contrast to other anti-hypertensive drugs such as diuretics and beta-blockers which may have a detrimental effect on insulin action, ACE-inhibitors appear to improve insulin action in **Type 2 diabetes** and essential hypertension, at least on a short-term basis.

5/7/84 (Item 1 from file: 50)
DIALOG(R)File 50:CAB Abstracts

02208325 CAB Accession Number: 901418379
Limitations of diet therapy in patients with non-insulin-dependent **diabetes** mellitus.
Wolffenbuttel, B. H. R.; Weber, R. F. A.; Koetsveld, P. M. van; Verschoor, L.
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International Journal of Obesity vol. 13 (2): p.173-182
Publication Year: 1989
ISSN: 0307-0565 --
Language: English
Document Type: Journal article
A total of 61 patients with noninsulin-dependent **diabetes** mellitus and fasting blood glucose of 12.0 plus or minus 0.6 mmol/litre were studied before and after dietary **treatment** as outpatients. At the

start of the study 33 patients were obese (body mass index more than 27.0 kg/m2); 20 were newly diagnosed and the median known duration of **diabetes** in the others was 5 years. beta -Cell function was measured by the release of C-peptide after intravenous injection of 1 mg **glucagon** (area under the curve of C-peptide = AUC-cp), as well as calculated according to the formulae of Matthews. Insulin action was estimated by measurement of fasting blood glucose, insulin and free fatty acid (FFA) concentrations. Non-obese patients showed more severe beta -cell deficiency than the obese (AUC-cp 2586 plus or minus 158 and 3294 plus or minus 277 pmol/litre 15 min), and did not improve in metabolic control during **treatment**. In the obese patients 3 response patterns to **treatment** were observed: weight loss and improvement in metabolic control accompanied primarily by increased beta -cell function or increased insulin action, or worsening of metabolic control. Those with less impaired beta -cell function and shorter known duration of **diabetes** showed the most favourable response. In conclusion, non-obese **type 2 diabetes** patients with fasting glucose above 10 mmol/litre do not improve on dietary **treatment** alone; in obese **type 2** diabetics weight reduction is essential and results in metabolic improvement, irrespective of the preceding fasting blood glucose concentrations. Improved beta -cell function as well as increased insulin action are responsible for this improvement. 25 ref.

5/7/85 (Item 2 from file: 50)
DIALOG(R)File 50:CAB Abstracts

01982764 CAB Accession Number: 881406951
Relationship between postheparin plasma lipases and high-density lipoprotein cholesterol in different types of **diabetes**.
Laakso, M.; Sarlund, H.; Ehnholm, C.; Voutilainen, E.; Aro, A.; Pyorala, K.
K. Pyorala, Dep. Medicine, Kuopio Univ. Central Hospital, 70210 Kuopio, Finland.
Diabetologia vol. 30 (9): p.703-706
Publication Year: 1987
ISSN: 0012-186X --
Language: English
Document Type: Journal article
Serum lipids, lipoproteins and post-heparin plasma lipases, lipoprotein lipase and hepatic lipase were estimated in 12 women with Type 1 (insulin-dependent) **diabetes** (post-**glucagon** C-peptide undetectable), in 11 insulin-**treated** women with **Type 2** (noninsulin-dependent) **diabetes** (post-**glucagon** C-peptide more than 0.60 nmol/litre) and in 16 non-diabetic control women. Those 3 groups of subjects were similar with respect to age and obesity. Insulin dose was similar in patients with Type 1 and with **Type 2 diabetes**. High-density lipoprotein (HDL) and HDL2 cholesterol were lower in patients with **Type 2 diabetes** than in non-diabetic controls but did not differ between patients with type 1 **diabetes** and non-diabetic controls. No difference in lipoprotein lipase activity was seen between the groups. The highest values of lipoprotein lipase and hepatic lipase activities were observed in patients with **Type 2 diabetes**. Lipoprotein lipase activity was correlated significantly with HDL cholesterol in patients with Type 1 **diabetes** and in patients with **Type 2 diabetes** but not in controls. Hepatic lipase activity was not correlated significantly with HDL cholesterol in any group. 22 ref.

5/7/86 (Item 3 from file: 50)

DIALOG(R)File 50:CAB Abstracts

01819973 CAB Accession Number: 871491076
Effects of weight loss on mechanisms of hyperglycemia in obese non-insulin-dependent **diabetes** mellitus.
Henry, R. R.; Wallace, P.; Olefsky, J. M.
Veterans Administration Medical Center, Medical Research Service (V-111G), 3350 La Jolla Village Drive, San Diego, CA 92161, USA.
Diabetes vol. 35 (9): p.990-998
Publication Year: 1986 --
Language: English
Document Type: Journal article
To assess the effects of weight loss on the mechanisms responsible for hyperglycaemia in noninsulin-dependent **diabetes** mellitus (**NIDDM**), 8 obese subjects with **NIDDM** were studied before and after weight reduction with further assessment after 3 weeks of isoenergetic (weight maintenance) refeeding. After weight loss of 16.8 plus or minus 2.7 kg (mean plus or minus s.e.), the fasting plasma glucose values decreased from 277 plus or minus 21 to 123 plus or minus 8 mg/100 ml. The individual fasting glucose values were highly correlated with the high basal rates of hepatic glucose output (HGO), which fell from 138 plus or minus 11 to 87 plus or minus 5 mg/m2 min after weight loss. The change in fasting plasma glucose was also correlated significantly with the change in the basal rates of HGO. That was associated with lower fasting serum **glucagon** values (from 229 plus or minus 15 to 141 plus or minus 12 pg/ml), less free fatty acids (from 791 plus or minus 87 to 379 plus or minus 35 mu Eq/litre) and unchanged basal insulin values (17 plus or minus 4 to 15 plus or minus 2 mu U/ml). Peripheral glucose disposal, assessed by the euglycaemic glucose-clamp technique, at insulin infusion rates of 120 and 1200 mU/m2 min, increased between 135 and 165%, from 128 plus or minus 17 to 288 plus or minus 24 mg/m2 min during the 120-mU/m2 min studies and from 159 plus or minus 19 to 318 plus or minus 24 mg/m2 min during the 1200-mU/m2 min clamp studies, despite comparable steady-state serum insulin values at each infusion rate before and after weight loss. HGO during the 120-mU/m2 min clamp studies increased from 85% to complete (100%) suppression after **treatment**. Adipocyte size was decreased 44% (851 plus or minus 91 to 475 plus or minus 48 pl), whereas surface area decreased by 32% (4.30 x 104 to 2.92 x 104 mu m2/cell). Insulin binding to isolated adipocytes was unchanged, whereas basal rates of 3-O-methylglucose transport in vitro increased from 0.21 plus or minus 0.13 to 0.53 plus or minus 0.24 pmol/(2 x 109 mu m2) x (10 s) and maximum glucose transport rates increased from 0.64 plus or minus 0.29 to 1.18 plus or minus 0.48 pmol/(2 x 105 cells) x (10 s) and 0.42 plus or minus 0.20 to 1.04 plus or minus 0.30 pmol/(2 x 109 mu m2) x (10 s). Absolute serum insulin values during oral glucose tolerance tests and meal tolerance tests were unchanged by weight reduction, whereas plasma glucose values were much lower. 45 ref.

5/7/87 (Item 4 from file: 50)
DIALOG(R)File 50:CAB Abstracts

01193452 CAB Accession Number: 811429903
The effect of **treatment** of **Type 2** (insulin independent) **diabetes** mellitus on plasma concentrations of pancreatic polypeptide and **glucagon**.
Berger, D.; Floyd, J. C., Jr.; Pek, S. B.
Univ. Michigan, C7009 Outpatient Bldg., Box 002, Ann Arbor, MI 48109, USA.
Diabetologia vol. 21 (2): p.120-125

Publication Year: 1981
ISSN: 0012-186X --
Language: English
Document Type: Journal article

In 8 patients with **Type 2** (insulin-independent) **diabetes** mellitus, the mean plus or minus s.e. mean fasting plasma glucose was 15.9 plus or minus 1.3 mmol/litre for 5 days of **treatment** and 5.9 plus or minus 0.4 mmol/litre for the last 5 days of **treatment** with diet plus insulin; corresponding fasting plasma pancreatic polypeptide values were 328 plus or minus 97 and 247 plus or minus 71 pg/ml and immunoreactive **glucagon** was 95 plus or minus 11 and 62 plus or minus 6 pg/ml. Cooked ground beef was given on the first day of diet **treatment** and on the last day of **treatment** with diet plus insulin; mean maximum increase of pancreatic polypeptide and total and incremental plasma pancreatic polypeptide response areas were significantly less after **treatment**, as was total area for immunoreactive **glucagon**. Return of fasting plasma glucose to normal by short-term **treatment** with diet plus insulin was associated with decreases in basal and stimulated secretory activity of the pancreatic polypeptide cells in insulin-independent **diabetes** mellitus. 20 ref.

5/7/88 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

05111166 EMBASE No: 1992251382
Estimation of plasma glucose fluctuation with a combination test of hemoglobin A(1c) and 1,5-anhydroglucitol

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Metabolism: Clinical and Experimental (METAB. CLIN. EXP.) (United States) 1992, 41/8 (862-867)
CODEN: METAA ISSN: 0026-0495
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We investigated the effect of plasma glucose fluctuation on hemoglobin A(1c) (HbA(1c)) and plasma 1,5-anhydroglucitol (AG) levels, especially in insulin-dependent **diabetes** mellitus (IDDM). Plasma AG is a new marker that provides sensitive and analytical information on glycemic control. The basic mechanisms underlying both the reduction and recovery of the plasma AG level, ie, the excretion into urine with glucosuria and the amount supplied to the body, were presumed to be similar in IDDM and non-insulin-dependent **diabetes** mellitus (**NIDDM**) patients. The correlation coefficient for mean plasma glucose and AG was -.591, and it was .578 for mean plasma glucose and HbA(1c) in IDDM patients. In **NIDDM**, the correlation between mean plasma glucose and AG was -.869, and between mean plasma glucose and HbA(1c), .875. The plasma AG levels in the IDDM group showed a lower range than in the **NIDDM** group, even with similar HbA(1c) levels. All the cases showing lower plasma AG levels among those with similar HbA(1c) levels manifested greater fluctuation of plasma glucose and a larger amount of urinary glucose. The lower AG level in IDDM patients was reversible to the level in **NIDDM** patients when the greater fluctuation of plasma glucose was corrected. Thus, it was suggested that because urinary glucose excretion is intermittently high in IDDM patients, plasma AG is frequently low, even though the mean plasma glucose and HbA(1c) levels suggest good control. The results of the present study indicate the significance of both plasma glucose fluctuation and mean plasma glucose level for an evaluation of glycemic control, especially in

IDDM patients, and imply the danger of frequent hypoglycemia if the improvement of glycemic control is evaluated by HbA(1c) alone.

5/7/89 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

05075540 EMBASE No: 1992215756
Intravenous infusion of diarginylinsulin, an insulin analogue: Effects on glucose turnover and lipid levels in insulin-**treated type II** diabetic patients
Monti L.D.; Poma R.; Caumo A.; Stefani I.; Picardi A.; Sandoli E.P.; Zoltobrocki M.; Micossi P.; Pozza G.
Department of Medicine, H.S. Raffaele Scientific Institute, via Olgettina 60,20132 Milano Italy
Metabolism: Clinical and Experimental (METAB. CLIN. EXP.) (United States) 1992, 41/5 (540-544)
CODEN: METAA ISSN: 0026-0495
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Diarginylinsulin is an intermediate in the conversion of proinsulin to insulin and is usually present in small amounts **in vivo** in humans. This study was designed to evaluate the following in insulin-**treated type II** diabetic patients: (1) the feasibility of an overnight intravenous infusion of diarginylinsulin, as compared with an overnight intravenous infusion of short-acting insulin, and the degree of early morning glycemic control; and (2) the effects of diarginylinsulin and human insulin on hepatic glucose production (HGO) in the postabsorptive state and on the glucose turnover rate and peripheral insulin sensitivity during an euglycemic hyperinsulinemic clamp. Diarginylinsulin and regular human insulin maintained a comparable degree of normoglycemia during the night, without significant glucose increases in the morning. Free-diarginylinsulin and free-insulin concentrations were not significantly different, and (HGO) was 2.1 +/- 0.5 versus 2.1 +/- 0.4 mg/kg/min with diarginylinsulin and regular human insulin, respectively (NS). During the euglycemic clamp, glucose infusion rate per unit of diarginylinsulin or human insulin infused (M/I ratio) was similar, and HGO was equally suppressed with diarginylinsulin and regular human insulin. No significant differences were seen in NEFA and triglyceride levels. In conclusion, these results indicate that diarginylinsulin is as potent as regular human insulin; it is normalizes HGO in the postabsorptive state; and its hepatic and peripheral actions on glucose and lipids are comparable to those of human insulin during an euglycemic hyperinsulinemic clamp.

5/7/90 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

05045943 EMBASE No: 1992186159
Sulfonylureas in **NIDDM**
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Fourth Department of Medicine, Helsinki University Hospital, Unioninkatu 38,SF-00170 Helsinki Finland
Diabetes Care (DIABETES CARE) (United States) 1992, 15/6 (737-754)
CODEN: DICAD ISSN: 0149-5992
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Sulfonylureas have represented the backbone of oral therapy in non-

insulin-dependent **diabetes** mellitus for >30 yr. Despite this, our knowledge about the mode of actions of these agents is limited, and the use of them is far from rational. Sulfonylureas lower blood glucose concentrations primarily by stimulating insulin secretion. The evidence for clinically significant extrapancreatic effects is scanty. Therefore, the effect of sulfonylurea is limited to patients with preserved beta-cell function, with the best effect observed in the early stages of the disease. Sulfonylurea **treatment** is often started relatively late and is continued when the agents can no longer achieve the **treatment** goals. Drug dosages are increased to maximum recommended doses, although there is no evidence for a dose-response relationship between the sulfonylurea dose and its biological effect: To rationalize the use of sulfonylureas, we should ask the questions to whom, how much, and for how long? The decision to stop **treatment** is as important as the decision to start **treatment**.

5/7/91 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

04971386 EMBASE No: 1992111602
Role of liver in pathophysiology of **NIDDM**
Consoli A.
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Diabetes Care (DIABETES CARE) (United States) 1992, 15/3 (430-441)
CODEN: DICAD ISSN: 0149-5992
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Glucose homeostasis is physiologically maintained by the balance between glucose production by the liver and glucose utilization by the peripheral tissues. Insulin controls hepatic glucose production and promotes glucose utilization by the skeletal muscle. In non-insulin-dependent **diabetes** mellitus (**NIDDM**), postabsorptive hepatic glucose production is increased and exhibits a positive correlation with fasting plasma glucose concentration. This increase in hepatic glucose production is the main cause of fasting hyperglycemia in **NIDDM**. Between the two processes by which the liver produces glucose (gluconeogenesis and glycogenolysis), gluconeogenesis appears to be drastically increased in **NIDDM**. The increase in gluconeogenesis accounts for most of the increased hepatic glucose production in this condition, and a positive correlation has been found in **NIDDM** subjects between the rates of gluconeogenesis and fasting plasma glucose concentration. Increased production of gluconeogenic precursors (lactate, alanine, glycerol) fuels this increased gluconeogenesis, but some type of intrahepatic mechanism is also present in **NIDDM** that increases the hepatic conversion of these substrates into glucose. Hyperglucagonemia and increased hepatic free fatty acid oxidation might be responsible for this increase hepatic gluconeogenic efficiency in **NIDDM**. Reduced suppression of hepatic glucose production after carbohydrate ingestion also plays an important role in the impairment in postprandial glucose homeostasis in **NIDDM**. In **NIDDM** subjects splanchnic extraction of an oral glucose load is not decreased, but hepatic glucose production is suppressed less than in nondiabetic subjects after the load. Residual hepatic glucose production after glucose ingestion is also correlated with fasting plasma glucose in **NIDDM**. Preliminary data suggest that in the postprandial state increased gluconeogenesis represents the primary mechanism responsible for impaired suppression of hepatic glucose production. Given the primary role of increase hepatic gluconeogenesis in the pathogenesis of hyperglycemia in **NIDDM**,

development of new drugs aimed at correcting the factors that might cause increased gluconeogenesis (e.g., increased free fatty acid oxidation and hyperglucagonemia) might open the way for new form of **treatment** of this disorder.

5/7/92 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

04844360 EMBASE No: 1991339096
Effect of an oral alphainf 2-adrenergic blocker (MK-912) on pancreatic islet function in non-insulin-dependent **diabetes** mellitus
Ortiz-Alonso F.J.; Herman W.H.; Gertz B.J.; Williams V.C.; Smith M.J.; Halter J.B.
Division of Geriatric Medicine, 300 N Ingalls,Ann Arbor, MI 48109 United States
Metabolism: Clinical and Experimental (METAB. CLIN. EXP.) (United States) 1991, 40/11 (1160-1167)
CODEN: METAA ISSN: 0026-0495
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We used MK-912, a potent new selective alphainf 2-adrenergic receptor antagonist that is active orally, to study the effect of short-term, selective alphainf 2-blockade on fasting plasma glucose (FPG) and pancreatic islet function in non-insulin-dependent **diabetes** (**NIDDM**). Ten asymptomatic patients with **NIDDM** received either a single oral dose of MK-912 (2 mg) or placebo in a double-blind, cross-over study. B-cell function was measured by the acute insulin response (AIR) to glucose (1.66 mmol/kg intravenously (IV)) and by the AIR to arginine (5 g IV) during a hyperglycemic glucose clamp at a mean glucose level of 32.1 mmol/L to provide an estimation of maximal B-cell secretory capacity. A-cell function was estimated by the acute **glucagon** response (AGR) to arginine during the glucose clamp. Effective alphainf 2-adrenergic blockade was apparently achieved, as there were substantial increases of plasma norepinephrine (NE) ($P < .01$) and both systolic blood pressure (SBP) ($P < .01$) and diastolic blood pressure (DBP) ($P < .05$) after **treatment** with MK-912, but not after placebo. MK-912 caused a significant ($P < .05$) although modest decrease of FPG that was associated with a small increase of fasting plasma insulin ($P < 0.01$), C-peptide ($P < .05$), and **glucagon** ($P < .01$). FPG and hormone levels remained unchanged after placebo. MK-912 tended to increase the AIR ($P = .06$) and the C-peptide response ($P = .07$) to glucose compared with placebo. There was a small, but significant, overall **treatment** effect for both the AIR and AGR to arginine with MK-912 (both $P < .05$, ANOVA). These studies indicate that MK-912 causes (1) sympathetic activation consistent with effective alphainf 2-adrenergic blockade; (2) a small decrease of FPG and a small increase of fasting plasma insulin; (3) a small improvement of B-cell function due to an increase in maximal B-cell secretory capacity; and (4) a small increase in basal and stimulated **glucagon**. These findings suggest that endogenous alphainf 2-adrenergic tone may contribute, although to a small extent, to the impaired B-cell function in **NIDDM**. If an alphainf 2-blocker becomes available that does not increase BP, studies would be warranted to evaluate its potential impact on glucose regulation in patients with **NIDDM**.

5/7/93 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

04801451 EMBASE No: 1991296187
Low-dose octreotide is able to cause a maximal inhibition of the glycemic responses to a mixed meal in obese **type 2** diabetic patients **treated** with insulin
Giustina A.; Girelli A.; Grazia Buffoli M.; Cimino A.; Legati F.; Valentini U.; Giustina G.
Cattedra di Clinica Medica, c/o 2a Medicina-Spedali Civili, 25125 Brescia Italy
Diabetes Research and Clinical Practice (DIABETES RES. CLIN. PRACT.) (Netherlands) 1991, 14/1 (47-54)
CODEN: DRCPE ISSN: 0168-8227
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH

5/7/94 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

04769355 EMBASE No: 1991264091
Compound M and B 39890A (N-(3-imidazol-1-ylpropyl)-2-(3-trifluoromethylbenzenesulphonamido)benzamide hydrochloride), a **glucagon** and insulin secretion inhibitor, improves insulin sensitivity in viable yellow obese-diabetic mice
Yen T.T.; Schmiegel K.K.; Gold G.; Williams G.D.; Dininger N.B.; Broderick C.L.; Gill A.M.
Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN 46285 United States
Archives Internationales de Pharmacodynamie et de Therapie (ARCH. INT. PHARMACODYN. THER.) (Belgium) 1991, 310/- (162-174)
CODEN: AIPTA ISSN: 0003-9780
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Compound M and B 39890A (N-(3-imidazol-1-ylpropyl)-2-(3-trifluoromethylbenzenesulphonamido)benzamide hydrochloride) had no effect on cellular cAMP and cGMP levels but significantly inhibited insulin and **glucagon** secretion from freshly isolated normal rat islets stimulated with 10 mM glucose and 20 mM arginine. Daily gavage of the compound for three days lowered the elevated blood glucose and plasma insulin levels in fed, male viable yellow obese-diabetic mice; the minimum effective dose was 25 mg/kg. However, M and B 39890A did not affect the blood glucose level of fasted diabetic mice. In addition, it had no effect on blood glucose levels of normal mice and streptozotocin-diabetic rats. M and B 39890A, fed in the diet at the concentration of 1 mg/g for 42 days, reversed the hyperglycemia of the fed diabetic mice without causing tachyphylaxis and improved the sensitivity to exogenous insulin as demonstrated by the lowering of blood glucose. When M and B 39890A was fed to young male mice destined to become diabetic, the development of hyperglycemia was prevented. Thus, M and B 39890A represents a new class of pharmacological agents that may prove to be effective for the chronic **treatment** of **type II** diabetics without the risk of hypoglycemia.

5/7/95 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE

04755847 EMBASE No: 1991249201
Hepatic sensitivity to insulin: Effects of sulfonylurea drugs
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2,35100 Padova Italy
American Journal of Medicine (AM. J. MED.) (United States) 1991, 90/SUPPL. 6A (29S-36S)
CODEN: AJMEA ISSN: 0002-9343
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Insulin regulation of hepatic glucose production (HGP) is altered in non-insulin-dependent **diabetes** mellitus (**NIDDM**), resulting in increased glucose output by the liver; this contributes to the elevation in plasma glucose concentration observed both in the basal state and postprandially. Therefore, restoration of normal insulin action in the liver must be a goal of hypoglycemic therapy. Sulfonylureas have been widely used for **treatment** of **NIDDM** over the past 30 years. In addition to their stimulatory effect on insulin secretion, these compounds seem to possess extrapancreatic effects. Early in vitro studies showed that addition of sulfonylureas to the perfusion medium of liver preparations could exert a significant suppressive effect on HGP. Subsequent experience suggested that these compounds could act at the level of the insulin receptor as well as at various postreceptor sites. These studies showed that sulfonylureas may inhibit glycogenolysis and gluconeogenesis while stimulating glycogen synthesis. Results obtained **in vivo** in **NIDDM** patients are in agreement with the in vitro studies. Long-term **treatment** with sulfonylureas is associated with a decline in fasting plasma glucose concentration and a parallel reduction in HGP. Nevertheless, the direct effect of sulfonylurea administration on the liver remains unclear, since the reduction in HGP that occurs during sulfonylurea **treatment** may be secondary to an overall improvement in insulin secretion. It is also of interest that in insulin-dependent diabetic patients, sulfonylurea administration in combination with insulin injections is not followed by a significant change in HGP. Possible effects of sulfonylureas on **glucagon** secretion and on the metabolism of free fatty acids (FFAs) may also contribute to improved sensitivity of the liver to the suppressive action of insulin, since these agents appear to reduce plasma **glucagon** and FFA concentrations. Thus, present data support an extrapancreatic action of sulfonylureas on the liver. However, it does appear that a certain degree of residual insulin secretion is required for sulfonylurea agents to elicit their hepatic effect.

04755844 EMBASE No: 1991249198
Mechanisms for hyperglycemia in **type II diabetes** mellitus: Therapeutic implications for sulfonylurea **treatment** - An update

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American Journal of Medicine (AM. J. MED.) (United States) 1991, 90/SUPPL. 6A (8S-14S)
CODEN: AJMEA ISSN: 0002-9343
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Non-insulin-dependent **diabetes** mellitus (**NIDDM**) is characterized by fasting hyperglycemia associated with defects in the pancreatic islet, the liver, and the peripheral tissues, which together comprise a feedback loop responsible for maintenance of glucose homeostasis. This review focuses on the key role of the endocrine pancreas

alpha and beta cells to coordinate glucose output from the liver with glucose utilization. The basal rate of hepatic glucose production is elevated in subjects with **NIDDM**, and this is positively correlated with the degree of fasting hyperglycemia. This increased rate of glucose release by the liver results from impaired hepatic sensitivity to insulin, reduced insulin secretion, and increased **glucagon** secretion. Though basal immunoreactive insulin levels in patients with **NIDDM** may appear normal when compared with healthy individuals, islet function testing at matched glucose levels reveals impairments of basal, steady-state,and stimulated insulin secretion due to a reduction in beta-cell secretory capacity and a reduced ability of glucose to suppress **glucagon**. The degree of impaired beta-cell responsiveness to glucose is closely related to the degree of fasting hyperglycemia but in a curvilinear fashion. The efficiency of glucose uptake by the peripheral tissues is also impaired due to a combination of decreased insulin secretion and defective cellular insulin action. This impairment becomes more important to the hyperglycemia as the islet alpha- and beta-cell function declines. Therapeutic interventions, to be effective, must reduce hepatic glucose production either by improving islet dysfunction and raising plasma insulin levels, or improving the effectiveness of insulin on the liver. Both result in a decline in the fasting glucose levels regardless of the cause of hyperglycemia. We conclude that **NIDDM** is characterized by a steady-state re-regulation of plasma glucose concentration at an elevated level in which islet dysfunction plays a necessary role. **Treatment** should be based on this physiologic understanding.

5/7/97 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE

04748135 EMBASE No: 1991241489
Acute diabetic complications
COMPLICATIONS AIGUES DU DIABETE
Medecine et Hygiene (MED. HYG.) (Switzerland) 1991, 49/1892 (1781-1790)
CODEN: MEHGA ISSN: 0025-6749
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: FRENCH SUMMARY LANGUAGE: ENGLISH

Acute diabetic complications are still frequent despite major efforts to educate diabetic patients. Hypoglycemia is the most common acute metabolic complication of **diabetes**. In patients **treated** by insulin, its frequency depends on the intensity of **treatment**. Ketoacidosis and hyperosmolar coma are characterized by hyperglycemia, volume and electrolyte depletion. In ketoacidosis, absolute insulin deficiency (type I **diabetes**) leads to massive lipolysis from adipose tissue generating free fatty acids which are eventually converted to ketone bodies by the liver. Acidosis results from ketone body accumulation. In **type II diabetes**, residual endogenous insulin secretion partially prevents lipolysis thereby limiting ketosis.

5/7/98 (Item 11 from file: 73)
DIALOG(R)File 73:EMBASE

04731449 EMBASE No: 1991224803
Non-insulin dependent diabetic patients have a progressively reduced insulin secretion in relation to the increased disease duration
Trischitta V.; Italia S.; Mazzarino S.; Frittitta L.; Favetta A.; Vigneri R.

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Diabetes, Nutrition and Metabolism - Clinical and Experimental (DIABETES NUTR. METAB. CLIN. EXP.) (Italy) 1991, 4/2 (107-111)
CODEN: DNMEE ISSN: 0394-3402
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Conflicting results have been reported on the possibility that a progressive deterioration of beta-cell function occurs in patients with non-insulin dependent **diabetes** mellitus (**NIDDM**). This paper reports a cross sectional study of C-peptide plasma levels after i.v. **glucagon** administration in 152 **NIDDM** patients. C-peptide values were negatively correlated ($p < 0.001$) with the duration of **diabetes** both in obese and non-obese patients. Moreover, when the 152 patients were subdivided into 4 quartiles (from quartile 1 to 4 depending on the increasing duration of **diabetes**), a significant ($p < 0.001$) and progressive decrease of C-peptide values was observed, with the highest values into quartile 1 and the lowest values into quartile 4. Finally, in a small group of 10 **NIDDM** patients, a longitudinal investigation was carried out by repeating C-peptide measurements 2 years after the first determination. Although the short term follow up period (only 2 years), C-peptide values were significantly lower ($p < 0.05$) at the second determination. The observed decrease of C-peptide values was independent of changes in fasting plasma glucose, body weight and antidiabetic **treatment**. All together these data support the possibility that in both obese and non-obese **NIDDM** patients a progressive deterioration of beta-cell secretory capacity takes place with increasing disease duration.

5/7/99 (Item 12 from file: 73)
DIALOG(R)File 73:EMBASE

04495735 EMBASE No: 1990387263
Partial recovery of insulin secretion and action after combined insulin-sulfonylurea **treatment** in **Type 2** (non-insulin-dependent) diabetic patients with secondary failure to oral agents
Del Prato S.; Vigili de Kreutzenberg; Riccio A.; Maifreni L.; Duner E.; Lisato G.; Iavicoli M.; Tiengo A.
Cattedra Malattie del Ricambio, Via Giustiniani, 2,I-35128 Padova Italy
Diabetologia (DIABETOLOGIA) (Germany) 1990, 33/11 (688-695)
CODEN: DBTGA ISSN: 0012-186X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Metabolic control, insulin secretion and insulin action were evaluated in seven **Type 2** (non-insulin-dependent) diabetic patients with secondary failure to oral antidiabetic agents before and after two months of combined therapy with supper-time insulin (Ultratard: 0.4 U/kg body weight/day) plus premeal glibenclamide (15 mg/day). Metabolic control was assessed by 24 h plasma glucose. NEFA, and substrate (lactate, alanine, glycerol, ketone bodies) profile. Insulin secretion was evaluated by **glucagon** stimulation of C-peptide secretion, hyperglycaemic clamp (+ 7mmol/l) and 24 h free-insulin and c-peptide profiles. The repeat studies, after two months of combined therapy, were performed at least 72 h after supper-time insulin withdrawal. Combining insulin and sulfonylurea agents resulted in a reduction in fasting plasma glucose (12.9 +/- 7 vs 10.4 +/- 1.2 mmol/l; $p < 0.05$) and hepatic glucose production (13.9 +/- 1.1 vs 11.1 +/- 1.1 mumol-kgsup -sup 1-minsup -sup 1; $p < 0.05$). Mean 24 h plasma

glucose was also lower (13.7 +/- 1.2 vs 11.1 +/- 1.4 mmol/l; p < 0.05). Decrements in fasting plasma glucose and mean 24 h profile were correlated (r = 0.90; p < 0.01). HbA(1c) also improved (11.8 +/- 0.8 vs 8.9 +/- 0.5%; p < 0.05). Twenty-four hour profile for NEFA, glycerol, and ketone bodies was lower after **treatment**, while no difference occurred in the blood lactate and alanine profile. Insulin secretion in response to **glucagon** (C-peptide = + 0.53 +/- 0.07 vs + 0.43 +/- 0.07 pmol/ml) and hyperglycaemia (free-insulin = 13.1 +/- 2.0 vs 12.3 +/- 2.2 mU/l) did not change. On the contrary, mean 24 h plasma free-insulin (13.2 +/- 2.6 vs 17.5 +/- 2.2 mU/l; p < 0.01) and C-peptide (0.76 +/- 0.10 vs 0.98 +/- 0.13 pmol/l; p < 0.02) as well as the area under the curve (19.1 +/- 4.1 vs 23.6 +/- 3.1 U/24 h; p < 0.01 and 1.16 +/- 0.14 vs 1.38 +/- 0.18 mumol/24 h; p < 0.02 respectively) were significantly increased. The ratio between glucose infusion (M) and plasma insulin concentration (I) during the hyperglycaemic clamp studies (M/I, an index of insulin sensitivity), was not statistically different (1.40 +/- 0.25 vs 1.81 +/- 0.40 mumol-kgsup -sup 1-minsup -sup 1/mU-lsup -sup 1). These data suggest that, in **Type 2** diabetic patients with secondary failure to oral antidiabetic agents, the combination of supper-time longacting insulin and premeal sulfonylurea agents can improve metabolc control. This positive effect is possibly mediated through an increased secretion of insulin in response to physiologic stimuli.

5/7/100 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE

04451756 EMBASE No: 1990339865
Combined therapy with glibenclamide and ultralente insulin in lean patients with **NIDDM** with secondary failure of sulfonylureas. Follow up at two years
TRAITEMENT COMBINE PAR LE GLIBENCLAMIDE ET L'INSULINE ULTRALENTE DANS L'ECHEC SECONDAIRE AUX SULFONYLUREES CHEZ LES PATIENTS DE POIDS NORMAL, SUIVI A DEUX ANS
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Diabete et Metabolisme (DIABETE METABOL.) (France) 1990, 16/4 (323-327)
CODEN: DIMED ISSN: 0338-1684
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: FRENCH; ENGLISH

Nine lean diabetic patients with secondary failure of oral hypoglycemic agents and with a poor residual insulin release under **treatment** with glibenclamide (15 mg/day) entered a cross-over study, in which ultralente insulin was **administered** alone or in combination with glibenclamide (15 mg/day). Combined therapy was accompanied by increased serum free-insulin levels and was more effective than glibenclamide alone on daily blood glucose profile, on glycosylated haemoglobin (HbA1C) and on Beta-OH butyrate; in 6 patients a near normalization of blood glucose control (daily blood glucose levels < 180 mg/dl) occurred. C peptide release, evaluated as daily profile and as response to i.v. **glucagon**, did not significantly change. When patients received insulin alone, daily blood glucose profile and HbA1C worsened, and serum free-insulin levels and C peptide release decreased, while Beta-OH butyrate levels remained low. These data indicate that combined therapy is effective since it maintains insulin release and enhances free insulin levels in insulinopenic patients. Four responders continued combined therapy for 2 years: the **treatment** was still effective and was accompanied by an increased C peptide release, probably due to persistent euglycemia.

5/7/101 (Item 14 from file: 73)
DIALOG(R)File 73:EMBASE

04351519 EMBASE No: 1990239582
The rationality and effectiveness of insulin therapy in elderly patients with **type II diabetes**
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Diabetologia Croatica (DIABETOL. CROAT.) (Yugoslavia) 1989, 18/4 (163-169)
CODEN: DBCRB ISSN: 0351-0042
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The aim of the study was to ascertain the rationality and effectiveness of insulin therapy in the **treatment** of **type II diabetes** and to ascertain whether there are any indications which would enable us to find out in which poorly controlled **type II** diabetics receiving a maximum daily dose of oral drugs is there a real failure of oral therapy and in which causes of poor metabolic functioning are to be sought elsewhere. We analyzed the data of 188 **type II** diabetics who were hospitalized because of suspected secondary drug failure. After a clinical trial it was established that 128 needed insulin (Group A), 28 insulin and oral antidiabetic drugs (Group C) and the remaining 34 could leave the hospital only on oral therapy (Group B). There were no significant difference ($p < 0,05$) between the groups as to the age of the patients, age duration of **diabetes**, BMI, C-peptide excreted in 24 hour urine, fasting serum C-peptide and serum C-peptide after a **glucagon** stimulation test. There were differences, however, in fasting glycemia and HbAinf 1. Results at 1, 6 and 12 months after discharge (*: results at admission): Group A: glycemia: 12,1 +/- 3,3*, 11,0 +/- 3,2*, 10,6 +/- 3,1* mmol/1; HbAinf 1: 11,3 +/- 1,6*, 9,2 +/- 1,4*, 9,1 +/- 1,5* %; Group B: glycemia: 11,4 +/- 4,0*, 12,5 +/- 3,3, 11,9 +/- 2,4 mmol/1; HbAinf 1: 9,4 +/- 1,2*, 9,9 +/- 2,1*. 10.3 +/- 1,4* %; Group C: glycemia: 10,3 +/- 2,9*, 11,3 +/- 2,7*, 11,6 +/- 3,0* mmol/1; HbAinf 1: 10,2 +/- 1,6*, 9,0 +/- 1,8*, 8,7 +/- 1,5* %. (*: statistically significant difference at $p < 0,05$). There were no statistical differences among the groups as far as glycemia and HbAinf 1 in different time periods. We conclude that a significant and longterm improvement of metabolic control occur in patients who had been switched to insulin because of a secondary drug failure, while improvement was only temporary in the group of patients in which the causes of poor metabolic functioning were elsewhere and so these patients could continue **treatment** with hypoglycemic drugs. Because of a high overlapping of results obtained in the groups due to high variance, unfortunately it is not possible to classify patients into either group merely on the basis of observed parameters without a clinical trial.

5/7/102 (Item 15 from file: 73)
DIALOG(R)File 73:EMBASE

04234565 EMBASE No: 1990117108
C-peptide but not insulin concentrations are related to the serum lipoprotein levels during insulin **treatment** of non-insulin-dependent **diabetes** mellitus (**NIDDM**) patients
Vessby B.; Boberg M.; Hellsing K.; Lithell H.; Berne C.
Department of Geriatrics, PO Box 12042, S-750 12 Uppsala Sweden

Diabetes Research (DIABETES RES.) (United Kingdom) 1989, 12/3 (109-116)
CODEN: DIREE ISSN: 0265-5985
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

In 21 non-insulin-dependent diabetic patients with secondary drug failure, once-daily long-acting insulin lead to a moderate improved metabolic control. At the conclusion of the study (eight months) the fasting blood glucose and HbA(1c) concentrations were significantly decreased, but the postprandial blood glucose concentrations in the afternoon were unaltered. The peripheral insulin sensitivity, as measured by the intravenous insulin tolerance test, and the lipoprotein lipase activity in adipose and skeletal muscle tissue had increased. After initiation of insulin therapy there was a transient decrease of the fasting and **glucagon**-stimulated C-peptide concentrations. The very low density lipoprotein lipids and apolipoprotein B, A-I and A-II were also reduced transiently. The only significant difference in lipoprotein composition at eight months compared with on admission, was an increased cholesterol and decreased triglyceride concentration in the high density lipoproteins. There were significant relationships between the C-peptide, but not the peripheral insulin, concentrations and the serum lipid concentrations. This may indicate that high peripheral insulin concentrations after administration of exogenous insulin may affect the hepatic lipoprotein production less than the portal insulin concentrations mainly derived from endogenous production.

5/7/103 (Item 16 from file: 73)
DIALOG(R)File 73:EMBASE

04016935 EMBASE No: 1989185977
A randomized crossover study of sulphonylurea and insulin **treatment** in patients with **Type 2 diabetes** poorly controlled on dietary therapy
Wolffenbuttel B.H.R.; Weber R.F.A.; Van Koetsveld P.M.; Weeks L.; Verschoor L.
Department of Internal Medicine III and Clinical Endocrinology, University Hospital 'Dijkzigt', Rotterdam Netherlands
Diabetic Medicine (DIABETIC MED.) (United Kingdom) 1989, 6/6 (520-525)
CODEN: DIMEE ISSN: 0742-3071
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

In 13 non-obese patients with **Type 2 diabetes** mellitus who failed to achieve adequate blood glucose control on dietary **treatment** (fasting blood glucose 13.4 +/- 2.7 (+/- SD) mmol lsup -sup 1, glycosylated haemoglobin 13.0 +/- 1.7%), the effects of 6 months insulin or sulphonylurea therapy on blood glucose control and lipid metabolism were compared in a randomized crossover study. Three patients, who showed a clear improvement on insulin (median glycosylated haemoglobin fell from 14.7 to 8.6%), withdrew from the study prematurely because of subjective and objective signs of hyperglycaemia after crossover from insulin to sulphonylurea. Daily dose after 6 months was 2000 mg tolbutamide (n = 3), 18 +/- 1 mg glibenclamide (n = 7), or 34 +/- 3 U insulin. On insulin, fasting (8.0 +/- 1.9 mmol lsup -sup 1) and postprandial blood glucose (10.4 +/- 2.7 mmol lsup -sup 1), and glycosylated haemoglobin (9.5 +/- 1.1%) were lower than on sulphonylurea (11.0 +/- 3.4 mmol lsup -sup 1, 14.4 +/- 4.8 mmol lsup -sup 1 and 11.0 +/- 2.5%, respectively, $p < 0.05$ in each case). Median increase in body weight was greater on insulin (4.2 vs 1.1 kg, $p < 0.05$). Six patients experienced improved well-being on insulin compared

with sulphonylurea. Median plasma non-esterified fatty acids decreased from 825 mumol lsup -sup 1 to 476 mumol lsup -sup 1 (sulphonylurea) and 642 mumol lsup -sup 1 (insulin, both $p < 0.05$). HDL cholesterol was higher after insulin (1.12 +/- 0.40 mmol lsup -sup 1) than after sulphonylurea (0.94 +/- 0.25 mmol lsup -sup 1, $p < 0.05$), and the LDL:HDL cholesterol ratio (3.27 +/- 1.07 vs 3.90 +/- 1.08) and VLDL triglycerides (0.67 +/- 0.22 vs 1.13 +/- 0.40 mmol lsup -sup 1) were lower (both $p < 0.05$). A C-peptide response after intravenous **glucagon** of below 5.0 nmol lsup -sup 1 15 min identified those patients who had better blood glucose control with insulin.

5/7/104 (Item 17 from file: 73)
DIALOG(R)File 73:EMBASE

04004933 EMBASE No: 1989173929
Effects of benfluorex in obese patients with metabolic disorders
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I Faculty of Medicine and Surgery, Universita degli Studi di Napoli, Napoli Italy
British Journal of Clinical Practice (BR. J. CLIN. PRACT.) (United Kingdom) 1989, 43/6 (201-208)
CODEN: BJCPA ISSN: 0007-0947
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Fifty obese (BMI=40.1+/-1.5) subjects (21 men and 21 women; average age 38.6+/-3.8 years) were prescribed a 600 cal/day diet (carbohydrates 30 g, proteins 60 g, lipids 10 g). Thirty patients were also given benfluorex (three tablets/day) for six months (Group A), whereas the other 20 patients (Group B) were **treated** with the dietary measures only. Apart from grade II and III obesity, several patients suffered from dyslipidaemia (Group A: n = 10; Group B: n = 7), non-insulin-dependent **diabetes** mellitus (**NIDDM**) (Group A: n = 4; Group B: n = 3) or IGT (Group A: n = 8; Group B: n = 6). The usual blood and biochemical tests and clinical examinations were carried out on Days 0, 90 and 180, together with the OGTT and **glucagon** test to determine blood glucose levels, IRI and CPR. There was no statistical difference between the weight loss of Group A and that of Group B. In Group A there was a statistically significant reduction ($p<0.001$) in total cholesterol, triglycerides, total/HDL-cholesterol and beta/alpha-lipoproteins and a significant increase in HDL-cholesterol and alpha-lipoproteins ($p>0.001$), wheas in Group B only a significant reduction in triglycerides ($p<0.001$) was observed. In **NIDDM** patients **treated** with benfluorex, normalisation of basal blood glucose levels was accompanied by an improvement in the OGTT blood glucose curve which was statistically significant relative to Group B. Benfluorex was well tolerated by all patients and no adverse event was reported. It was possible therefore to demonstrate the intrinsic effects of benfluorex independently of the weight loss, in particular the euglycaemic effect of this drug in obese diabetics, and its efficacy in normalising blood lipids and reducing the atherogenic risk factors in obese patients. The safety of benfluorex at a dosage of three tablets/day was confirmed.

5/7/105 (Item 18 from file: 73)
DIALOG(R)File 73:EMBASE

03992415 EMBASE No: 1989161411
Islet cell antibodies and insulin autoantibodies in patients **treated** with oral hypoglycaemic agents

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Diabetic Medicine (DIABETIC MED.) (United Kingdom) 1989, 6/5 (434-439)
CODEN: DIMEE ISSN: 0742-3071
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Clinical and immunological features suggesting Type 1 **diabetes** were assessed in 202 patients **treated** with oral hypoglycaemic agents for presumed **Type 2 diabetes**. Islet cell antibodies (ICA) were detected at a level exceeding 5 JDF units in 5.9% of patients, and complement-fixing ICA were detected in 3.4%. IgG insulin autoantibodies were detected in 8.8% of insulin-naive patients, none of whom were ICA positive. ICA were detected more frequently in patients with shorter duration of **diabetes** ($p = 0.02$). Age and relative body weight were similar in ICA positive and negative groups. ICA positive patients were more likely to have lost weight ($p < 0.02$) than ICA negative patients, although this may have been attributable to the differing duration of **diabetes** in the two groups. Other individual clinical features suggesting Type 1 **diabetes** were not significantly more frequent in ICA positive patients. However, a higher proportion of ICA positive than ICA negative patients had one or more features suggestive of Type 1 **diabetes** irrespective of the duration of **diabetes**. Clinical features suggesting **Type 2 diabetes** were present in a similar proportion of ICA positive and ICA negative patients. Fasting and **glucagon** stimulated C-peptide levels were similar in ICA positive and matched ICA negative patients.

5/7/106 (Item 19 from file: 73)
DIALOG(R)File 73:EMBASE

03983365 EMBASE No: 1989152361
Physiological bases for the **treatment** of the physically active individual with **diabetes**
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Department of Molecular Physiology and Biophysics, Vanderbilt University School of Medicine, Nashville, TN 37232 United States
Sports Medicine (SPORTS MED.) (New Zealand) 1989, 7/6 (376-392)
CODEN: SPMEE ISSN: 0112-1642
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Substrate utilisation and glucose homeostasis during exercise is controlled by the effects of precise changes in insulin, **glucagon** and the catecholamines. The important role these hormones play is clearly seen in people with **diabetes**, as the normal endocrine response is often lost. In individuals with insulin-dependent **diabetes** (IDDM), there can be an increased risk of hypoglycaemia during or after exercise or, conversely, there can be a worsening of the diabetic state if insulin deficiency is present. In contrast, it appears that people with non-insulin-dependent **diabetes** (**NIDDM**) can generally exercise without fear of a deleterious metabolic response. The exercise response both in healthy subjects and in those with **diabetes** is dependent on many factors such as age, nutritional status and the duration and intensity of exercise. Since there are so many variables which govern individual response to exercise, an exact exercise prescription for all people with **diabetes** cannot be made. There are many adjustments to the therapeutic regimen which an individual with IDDM can make in order to

avoid hypoglycaemia during or after exercise. In general, a reduction in insulin dosage and the added ingestion and continual availability of carbohydrates are wise precautions. On the other hand, exercise should be postponed if blood glucose is greater than 2500 mg/L and ketones are present in the urine. As more is understood about the regulation of substrate metabolism during exercise, more refined therapeutic strategies can be defined. An understanding of the metabolic response to exercise is critical for generating an effective and safe training programme for all diabetic individuals who wish to be physically active.

5/7/107 (Item 20 from file: 73)
DIALOG(R)File 73:EMBASE

03971067 EMBASE No: 1989140063
Secondary failure to oral hypoglycaemic agents in non-obese patients with non-insulin-dependent **diabetes** is related to reduced insulin release
Pontiroli A.E.; Calderara A.; Maffi P.; Bonisolli L.; Carenini A.; Piatti P.M.; Monti L.D.; Gallus G.; Pozza G.; Illeni M.T.
Istituto Scientifico Ospedale San Raffaele, Cattedra di Clinica Medica, Universita' di Milano, 20132 Milano Italy
Diabete et Metabolisme (DIABETE METABOL.) (France) 1989, 15/2 (79-84)
CODEN: DIMED ISSN: 0338-1684
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: FRENCH; ENGLISH

The frequency of secondary failure to oral hypoglycaemic agents (OHA) in patients with non-insulin dependent **diabetes** (**NIDDM**) is still unknown, despite more than 30 years of use of OHA. The term secondary failure should be limited to patients who, despite maximal dosages of OHA and despite full compliance with diet and therapy, are no longer controlled and require insulin to obtain an acceptable glucose metabolism. We evaluated 248 out-patients, either on OHA, or on insulin because of poor metabolic control with OHA, in order to assess duration of **treatment** with OHA since diagnosis, by means of actuarial curves (Mantel-Cox test). Patients with low relative body weight (RBW <=100) experienced secondary failure earlier and more often than obese patients (RBW >120) or overweight (RBW 101-120) patients. In 66 of the above out-patients, 33 OHA-**treated** and 33 insulin-**treated**, matched for age at onset and duration of disease, islet-cell-antibodies (ICA) and C-peptide release at fasting, 6 min after i.v. **glucagon** and post prandially were evaluated. Only among lean and overweight patients, was C-peptide release significantly lower in insulin-**treated** than in OHA-**treated** patients; differences disappeared in obese patients. ICA were found in only 7 patients (10.6%). HLA phenotype was different from that of healthy blood donors for the loci HLA B5, B13, CW4, with no differences between OHA-**treated** and insulin-**treated** patients. These data indicate that secondary failure is more frequent in lean patients with **NIDDM**, and is related to reduced insulin release.

5/7/108 (Item 21 from file: 73)
DIALOG(R)File 73:EMBASE

03923284 EMBASE No: 1989092277
Elevated plasma glucose and lowered triglyceride levels from omega-3 fatty acid supplementation in **type II diabetes**
Friday K.E.; Childs M.T.; Tsunehara C.H.; Fujimoto W.Y.; Bierman E.L.; Ensinck J.W.
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Diabetes Care (DIABETES CARE) (United States) 1989, 12/4 (276-281)
CODEN: DICAD ISSN: 0149-5992
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We studied the effect of omega-3 fatty acids (omega3FA) on glucose homeostasis and lipoprotein levels in eight **type II** (non-insulin-dependent) diabetic subjects ingesting 8 g/day omega3FA for 8 wk as marine-lipid concentrate capsules. After omega3FA supplementation, fasting plasma glucose levels increased 22% (P = .005) and meal-stimulated glucose increased 35% (P = .036. The percentage of glucose elevation correlated with percentage ideal body weight (r = .73, P = .04). No significant changes were seen in fasting or meal-stimulated plasma insulin, glucose disposal, or insulin-to-**glucagon** ratios. Very-low-density lipoprotein cholesterol and triglyceride (TG) levels showed consistent reductions of 56% (P < .001) and 42% (P < .001), respectively, after omega3FA supplementation. Total cholesterol levels decreased 7% (P <.05) without alteration in low- or high-density lipoprotein cholesterol. Thus, omega3FA supplementation at a dose of 8 g/day significantly improves plasma TG levels but increases fasting and meal-stimulated glucose concentrations in the **type II** diabetic patient not **treated** with insulin or sulfonylurea agents. Marine-lipid concentrate capsules supplying large amounts of omega3FAs should be used cautiously in the **type II** diabetic patient.

5/7/109 (Item 22 from file: 73)
DIALOG(R)File 73:EMBASE

03891494 EMBASE No: 1989060450
Clinical value of the C-peptide response to **glucagon** stimulation in the choice of **treatment** for poorly controlled **type II** diabetics
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Zdravstveni Vestnik (ZDRAV. VESTN.) (Yugoslavia) 1988, 57/11-12 (417-419)
CODEN: ZDVEA ISSN: 0350-0063
DOCUMENT TYPE: Journal
LANGUAGE: SLOVENE SUMMARY LANGUAGE: ENGLISH

5/7/110 (Item 23 from file: 73)
DIALOG(R)File 73:EMBASE

03889854 EMBASE No: 1989058810
Somatostatin analogues in **diabetes** mellitus
Davies R.R.; Turner S.J.; Alberti K.G.M.M.; Johnston D.G.
Ninewells Hospital and Medical School, Dundee DD1 9SY United Kingdom
Diabetic Medicine (DIABETIC MED.) (United Kingdom) 1989, 6/2 (103-111)
CODEN: DIMEE ISSN: 0742-3071
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Growth hormone (GH) has long been considered to have importance in **diabetes**. With poor control in Type 1 **diabetes** GH levels are high and may aggravate poor metabolic control. Pharmacological suppression of Gh release at this stage might reverse the metabolic changes, with the

possible added benefit of lower plasma insulin concentrations. Diabetic patients with life-long GH deficiency rarely develop retinopathy, while pituitary ablation in patients with retinopathy often leads to improvement. Growth hormone releaseng inhibiting factor, somatostatin, has a short plasma half-life, and multiple effects on the endocrine system and on the gastrointestinal tract, making it unsuitable for clinical use as a GH suppressant. Long-acting analogues have a long half-life, but remain non-specific in their effects. In **Type 2 diabetes** the analogue Octreotide suppresses insulin and **glucagon** release, leaving glucose levels either unchanged or somewhat elevated. Gastrointestinal side-effects have been common, but may diminish with long-term **treatment**. In Type 1 **diabetes** insulin requirement is decreased by Octreotide, but as in **Type 2 diabetes** GH suppression has been observed consistently only when the drug was given at bed-time. The decrease in insulin requirement may reflect suppression of **glucagon** release and/or gut effects. Amelioration of the 'dawn phenomenon' has not proved possible, and hypoglycaemia has proved a particular problem with Octreotide given subcutaneously at night. The lack of effective GH suppression (particularly in patients with proliferative retinopathy), lack of specificity, and the gut and hypoglycaemic-side-effects, argue strongly against a clinical role for the current somatostatin analogues in **diabetes** mellitus.

5/7/111 (Item 24 from file: 73)
DIALOG(R)File 73:EMBASE

03835988 EMBASE No: 1989004942
Glucose counterregulation and its impact on **diabetes** mellitus
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University of Pittsburgh School of Medicine, Clinical Research Center, Pittsburgh, PA United States
Diabetes (DIABETES) (United States) 1988, 37/12 (1608-1617)
CODEN: DIAEA ISSN: 0012-1797
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Glucose counterregulation is the sum of processes that protect against development of hypoglycemia and that restore euglycemia if hypoglycemia should occur. In order of importance, the key counterregulatory factors are **glucagon**, epinephrine, growth hormone, cortisol, and hepatic autoregulation. These act primarily by increasing hepatic glucose output, initially via breakdown of glycogen and later by gluconeogenesis. In people without **diabetes** and in people with **type II** (non-insulin-dependent) **diabetes**, suppression of endogenous insulin secretion during hypoglycemia is also important in permitting full expression of the effects of counterregulation. People with **diabetes** are more prone to develop hypoglycemia for various reasons (e.g., insulin overdose, skipped meals, and intensive exercise); one that has recently been identified is impaired glucose counterregulation: patients with type I (insulin-dependent) **diabetes** (and to a lesser extent, patients with **type II diabetes**) lose the **glucagon** response to hypoglycemia; subsequent development of autonomic neuropathy with concomitant loss of the epinephrine response leads to almost complete paralysis of counterregulation and loss of recognition of hypoglycemia. To make matters worse, an episode of hypoglycemia that causes activation of counterregulation can lead to rebound hyperglycemia (Somogyi phenomenon); if this is improperly **treated**, brittle **diabetes** may follow. Thus, abnormalities in glucose counterregulation may predispose to severe hypoglycemia and prevent achievement of optimal glycemic control in patients with **diabetes**.

5/7/112 (Item 25 from file: 73)
DIALOG(R)File 73:EMBASE

03832452 EMBASE No: 1989001406
Pancreatic B-cell function in non-insulin-dependent **diabetes** mellitus during successive periods of sulfonylurea and insulin **treatment**: Serum C-peptide response to **glucagon** and urine C-peptide excretion
Hsieh S.D.; Iwamoto Y.; Matsuda A.; Kuzuya T.
Division of Endocrinology and Metabolism, Jichi Medical School, Tochigi-ken 329-04 Japan
Endocrinologia Japonica (ENDOCRINOL. JPN.) (Japan) 1987, 34/4 (561-567)
CODEN: ECJPA ISSN: 0013-7219
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Serum C-peptide responses to **glucagon** and daily urine C-peptide excretion in successive periods of different **treatment** in two groups of patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) (mean interval between two tests < 1 month) were compared. In group A patients (n = 8), the glycemic control was improved after transferring the **treatment** from sulfonylurea (SU) to insulin (fasting plasma glucose: SU : 192 +/- 47, insulin: 127 +/- 21 mg/dl, mean +/- S.D., p < 0.01). Fasting serum C-peptide immunoreactivity (CPR) was significantly lower at the period of insulin **treatment** (SU: 1.93 +/- 1.01, insulin: 1.47 +/- 0.79 ng/ml, < 0.05), but there was no difference in the increase in serum CPR (maximal - fasting) (Delta serum CPR) during **glucagon** stimulation in the two periods of **treatment** (SU: 1.70 +/- 0.72, insulin: 1.47 +/- 0.98 ng/ml). In group B patients (n = 7), there was no significant difference in glycemic control after transferring the **treatment** from insulin to SU (fasting plasma glucose: insulin: 127 +/- 24, SU: 103 +/- 13 mg/dl). Fasting serum CPR was significantly lower during the period of insulin **treatment** (insulin: 1.39 +/- 0.64, SU: 2.21 +/- 0.86 ng/ml, p < 0.025), but Delta serum CPR during **glucagon** stimulation still showed no significant different between the two periods (insulin: 1.97 +/- 1.16, SU: 2.33 +/- 1.57 ng/ml). On the other hand, daily urine CPR excretion was constantly lower during insulin **treatment** than during SU **treatment** in both groups (group A: SU: 65.6 +/- 23.2, insulin: 37.1 +/- 15.3 mug, p < 0.01, group B: insulin: 40.3 +/- 14.7, SU: 65.6 +/- 12.4 mug, p < 0.01). The data suggest that basal and daily pancreatic B-cell secretion in **NIDDM** patients varies within the short periods of different **treatment**. However, the CPR response to **glucagon** remains stable.

5/7/113 (Item 26 from file: 73)
DIALOG(R)File 73:EMBASE

03770301 EMBASE No: 1988219737
Effect of a new long-acting somatostatin analogue (SMS 201-995) on glycemic and hormonal profiles in insulin-**treated type II** diabetic patients
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Istituto di Patologia Medica, Universita di Brescia, 25100 Brescia Italy
Journal of Endocrinological Investigation (J. ENDOCRINOL. INVEST.) (Italy) 1988, 11/7 (501-507)
CODEN: JEIND ISSN: 0391-4097

DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Five **type II** diabetic patients were studied after secondary failure of oral agents, wtih and without the addition of the new long-acting somatostatin analogue SMS 201-995 to an intermediate-acting insulin regimen. SMS 201-995 was **administered** twice daily, before breakfest and dinner, as 100 mug sc injections, and resulted in a lowering of plasma glucose, as well as of plasma **glucagon** and serum C-peptide levels. SMS 201-995 abolished postprandial glycemic and xylosemic peaks related to meals and to oral d-xylose when they were taken shortly after the administration of the analogue, while it had no effect on glycemic and xylosemic increments that followed the midday meal. The new somatostatin analogue improves glucose tolerance in **type II** diabetic patients, both by inhibiting counteregulatory hormones and by delaying and reducing intestinal absorption of nutrients. Its administration could lead to a reduction of daily insulin requirements. Our findings indicate that SMS 201-995 may have a role as an adjuct to insulin in the management of **type II** diabetic patients after secondary failure of oral agents.

5/7/114 (Item 27 from file: 73)
DIALOG(R)File 73:EMBASE

03718839 EMBASE No: 1988168275
Oxytocin increases arginine-induced A and B cell secretion in normal man and in diabetic subjects
Paolisso G.; Sgambato S.; Passariello N.; Giugliano D.; Torella R.; Memoli P.; Varricchio M.; D'Onofrio F.
Istituto di Gerontologia e Geriatria, 1st Medical School, University of Naples, Naples Italy
Diabete et Metabolisme (DIABETE METABOL.) (France) 1988, 14/2 (104-107)
CODEN: DIMED ISSN: 0338-1684
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: FRENCH; ENGLISH

In previous in vitro and **in vivo** studies oxytocin was shown to stimulate A and B cell secretion. In the present study we show that oxytocin is also able to increase arginine-induced **glucagon** and insulin secretion in healthy human beings. Similar results were obtained in both insulin-dependent (type-1) and non-insulin dependent (**type-2**) diabetic subjects.

5/7/115 (Item 28 from file: 73)
DIALOG(R)File 73:EMBASE

03710531 EMBASE No: 1988159967
Response to single dose of aspartame or saccharin by **NIDDM** patients
Horwitz D.L.; McLane M.; Kobe P.
Department of Medicine, University of Illinois at Chicago, Chicago, IL 60680 United States
Diabetes Care (DIABETES CARE) (United States) 1988, 11/3 (230-234)
CODEN: DICAD ISSN: 0149-5992
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Twelve normal subjects and 10 subjects with non-insulin-dependent

diabetes mellitus were given, in random order at intervals of >=1 wk, three drinks of the same beverage: one unsweetened, one sweetened with 400 mg aspartame, and one sweetened with 135 mg saccharin. The amount of sweetener approximated that of 1 L of sugar-free soft drink. Plasma glucose, insulin, and **glucagon** were measured for 3 h after ingestion of the test beverage. Plasma glucose declined slightly throughout the test period, probably due to fasting, with no differences between the three **treatments**. Neither sweetener affected peak insulin levels in subjects with or without **diabetes**. Analysis of area under the curve showed that mean insulin levels were statistically significantly higher after aspartame than after saccharin or unsweetened beverage in normal subjects only, but the magnitude of the difference was small and unlikely to be of physiological importance in the absence of differences in glucose levels. Furthermore, the differences could largely be accounted for by a decrease in insulin values after both unsweetened beverage and saccharin, with no change from baseline after aspartame. **Glucagon** levels showed time-to-time variation but no overall differences. We conclude that ingestion of aspartame- or saccharin-sweetened beverages by fasting subjects, with or without **diabetes**, did not affect blood glucose homeostasis.

5/7/116 (Item 29 from file: 73)
DIALOG(R)File 73:EMBASE

03682031 EMBASE No: 1988131467
Effects of the combination of insulin and glibenclamide in **Type 2** (non-insulin-dependent) diabetic patients with secondary failure to oral hypoglycaemic agents
Stenman S.; Groop P.-H.; Saloranta C.; Totterman K.J.; Fyhrqvist F.; Groop L.
Fourth Department of Medicine, Helsinki University Central Hospital, SF-00190 Helsinki Finland
Diabetologia (DIABETOLOGIA) (Germany) 1988, 31/4 (206-213)
CODEN: DBTGA ISSN: 0012-186X
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The effects of combined insulin and sulfonylurea therapy on glycaemic control and B-cell function was studied in 15 **Type 2** (non-insulin-dependent) diabetic patients who had failed on **treatment** with oral hypoglycaemic agents. The patients were first **treated** with insulin alone for four months. Five patients were given two daily insulin doses and ten patients one dose. During insulin **treatment** the fasting plasma glucose fell from 14.5 +/- 0.8 to 8.8 +/- 0.4 mmol/l and the HbAinf 1 concentration from 12.6 +/- 0.4 to 9.2 +/- 0.2%. This improvement of glycaemic control was associated with a suppression of basal (from 0.31 +/- 0.04 to 0.10 +/- 0.02 nmol/l) and **glucagon**-stimulated (from 0.50 +/- 0.08 to 0.19 +/- 0.04 nmol/l) C-peptide concentrations. Four months after starting insulin therapy the patients were randomised to a four-month double-blind cross-over **treatment** with insulin combined with either 15 mg glibenclamide per day or with placebo. Addition of glibenclamide to insulin resulted in a further reduction of the fasting plasma glucose (7.9 +/- 0.5 mmol/l) and HbAinf 1 (8.3 +/- 0.2%) concentration whereas the basal (0.21 +/- 0.03 nmol/l) and **glucagon**-stimulated C-peptide concentrations (0.34 +/- 0.06 nmol/l) increased again. Additional of placebo to insulin had no effect. The daily insulin dose could be reduced by 25% after addition of glibenclamide to insulin, while it remained unchanged when insulin was combined with placebo. The fasting free insulin concentration did not differ between the glibenclamide and placebo periods (28 +/- 6 vs 30 +/- 5 mmol/l). The fasting free insulin concentration

correlated, however, positively with the insulin dose ($r = 0.76$, $p < 0.01$) indicating that the insulin dose was the main determinant of the free insulin concentration. In contrast, the basal C-peptide concentration was higher during the insulin plus glibenclamide than during the insulin plus placebo period (0.21 +/- 0.03 vs 0.16 +/- 0.03 nmol/l; $p < 0.05$). Addition of glibenclamide to insulin therapy increased the **treatment** cost by 30-50%, was associated with increased frequency of mild hypoglycaemic reactions and with a slight, but significant fall in HDL cholesterol concentration (from 1.40 +/- 0.07 to 1.29 +/- 0.06; $p < 0.05$) compared with insulin plus placebo. We conclude that in **Type 2** diabetic patients, who have failed on **treatment** with oral hypoglycaemic agents, the combination of insulin and glibenclamide resulted in slightly improved glycaemic control and allowed reduction of the insulin dose. The price for this improvement was higher **treatment** costs, more (mild) hypoglycaemic reactions and a marginal fall in the HDL cholesterol concentration. Whether the same effect could have been achieved with divided insulin doses in all patients is not known.

5/7/117 (Item 30 from file: 73)
DIALOG(R)File 73:EMBASE

03668018 EMBASE No: 1988117454
Hypoglycemia - Mechanisms and prevention in **NIDDM treatment** with insulin
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Fondation pour Recherches Medicales, 1211 Geneva 4 Switzerland
Diabetes Research and Clinical Practice (DIABETES RES. CLIN. PRACT.) (Netherlands) 1988, 4/SUPPL. 1 (62-65)
CODEN: DRCPE ISSN: 0168-8227
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

In conclusion, hypoglycemia is a permanent danger of insulin therapy in **NIDDM**. The quality of special education received by physicians, health care providers and patients is unmistakably the guide to an improved prevention.

5/7/118 (Item 31 from file: 73)
DIALOG(R)File 73:EMBASE

03668014 EMBASE No: 1988117450
Secondary failure of oral antidiabetic and dietetic therapy in non-insulin-dependent **diabetes** mellitus. Remission through short sessions of continuous intravenous insulin infusion
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Endocrine and Metabolic Diseases Clinic, Lapeyronie Hospital, F-34059 Montpellier France
Diabetes Research and Clinical Practice (DIABETES RES. CLIN. PRACT.) (Netherlands) 1988, 4/SUPPL. 1 (41-46)
CODEN: DRCPE ISSN: 0168-8227
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The infusion of periodic intravenous insulin for the equilibrium of the diabetic state is proposed for cases of non-insulin-dependent **diabetes** mellitus (**NIDDM**) that have become resistant to oral **treatment**. In order to re-establish the efficacy of oral antidiabetic **treatment**, 37 patients with **NIDDM** presenting secondary failure

to diet and oral antidiabetic therapy were subjected to sessions of continuous intravenous insulin infusion, resulting in transitory normal blood sugars. With a diminution of symptoms, an increase in the efficacy of oral **treatment** was noted in 18 cases (48.6%), allowing the continuation of **treatment** without disturbance of the equilibrium over periods of 6 and 12 months. This improvement is not concurrent with the rise in **glucagon**-stimulated insulin secretion as evidenced by C-peptiduria and basal C-peptidemia. An improvement in insulin sensitivity (not investigated in this study) might explain this beneficial effect. Periodic intravenous infusions of insulin, based on the diabetic equilibrium, are proposed for the **treatment** of **NIDDM** patients that have become resistant to oral therapy.

5/7/119 (Item 32 from file: 73)
DIALOG(R)File 73:EMBASE

03667133 EMBASE No: 1988116569
Biochemical changes in rhesus monkey during the first days after streptozotocin administration are indictive of selective beta cell destruction
Takimoto G.; Jones C.; Lands W.; Bauman A.; Jeffrey J.; Jonasson O.
Department of Surgery, University of Illinois College of Medicine, Chicago, IL United States
Metabolism: Clinical and Experimental (METAB. CLIN. EXP.) (United States) 1988, 37/4 (364-370)
CODEN: METAA ISSN: 0026-0495
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Hormonal and glycemic changes in 22 rhesus monkeys were characterized during the first days after **treatment** with streptozotocin (STZ) (45 to 55 mg/kg, **administered** intravenously (IV)). Almost half (10/22) of the monkeys developed insulin-dependent **diabetes** mellitus (STZ-IDDM) within five days following injection. Four of the remaining monkeys did not become insulin dependent for at least 6 months after STZ **treatment**, during which time they were considered non-insulin-dependent, and eight monkeys never required exogenous insulin. In the STZ-IDDM group, plasma immunoreactive c-peptide (IRC-P) levels fell by three hours after STZ from a mean +/- SEM of 252 +/- 82 to 101 +/- 45 pg/mL, as glucose and immunoreactive **glucagon** (IRG) levels increased from 65 +/- 3 and 120 +/- 37, respectively, to 336 +/- 43 mg/dL and 234 +/- 52 pg/mL, respectively. Between six and 30 hours after **treatment**, IRC-P increased to a peak of 1,561 +/- 360 pg/mL before falling permanently to < 60 pg/mL by 66 hours. During this period, glucose and IRG responded in a reciprocal fashion by falling and then increasing to levels above 300 mg/dL and 300 pg/mL, respectively, by 66 hours. In the non-insulin-dependent **diabetes** mellitus (STZ-**NIDDM**) group, no clear reciprocal relationship between IRC-P and glucose and IRG was obtained. In nine additional monkeys subjected to total pancreatectomy (Px), IRC-P and IRG levels fell immediately and permanently by > 90% and 75%, respectively. Levels of immunoreactive somatostatin increased steadily over the initial 96 hours following STZ, but did so in both STZ-IDDM and Px monkey groups. Plasma lipid hydroperoxide levels measured in two monkeys that developed STZ-IDDM were unchanged during the first 96 hours after STZ administration. In conclusion, the glycemic and hormonal pattern observed with STZ-IDDM rhesus monkeys during the first days following **treatment** is indicative of selective pancreatic beta-cell destruction resulting from a direct action of STZ.

5/7/120 (Item 33 from file: 73)
DIALOG(R)File 73:EMBASE

03569380 EMBASE No: 1988018816
The dawn phenomenon: Nocturnal blood glucose homeostatis in insulin-dependent **diabetes** mellitus
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Diabetic Medicine (DIABETIC MED.) (United Kingdom) 1988, 5/1 (13-21)
CODEN: DIMEE ISSN: 0742-3071
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Strictly defined, the dawn phenomenon is transient decrease in hepatic insulin sensitivity occurring in the early morning hours in patients with type 1 **diabetes** mellitus in the absence of preceding hypoglycaemia and concomitant hypoinsulinaemia. Consequently, the insulin requirements to prevent hyperglycaemia are greater (by approximately 30%) at dawn, as compared with the early part of the night. A dawn phenomenon also occurs in patients with **type 2 diabetes** as well as in normal subjects. In normal subjects insulin secretion increases at dawn, and the plasma glucose concentration does not therefore rise. In patients, by contrast, insulin bioavailability cannot increase, and plasma glucose concentration therefore rises by 3-4 mmol/l. The dawn phenomenon is not the sole cause of fasting hyperglycaemia in diabetic patients. Insulin deficiency after 0300-0400 h (due to the dissipation of depot-insulin preparations injected in the evening) greatly exaggerates any dawn hyperglycaemia. Nocturnal hypoglycaemia may also result in exaggerated fasting as well as post-breakfast hyperglycaemia by inducing hepatic and extrahepatic insulin resistance (Somogyi phenomenon). Specific **treatment** of the dawn phenomenon is generally not necessary, since it usually produces only modest hyperglycaemia, but the factors associated with hyperglycaemia at dawn, namely preceding nocturnal hypoglycaemia and insulin deficiency in the early morning (common in patients **treated** with either intermediate-acting insulin in the evening or fixed-rate CSII) should be tackled where possible. Currently such a goal is only feasible with the physiological approach of overnight insulin delivery by CSII at variable rate.

5/7/121 (Item 34 from file: 73)
DIALOG(R)File 73:EMBASE

03514081 EMBASE No: 1987031017
Selective unresponsiveness of pancreatic beta-cells to acute sulfonylurea stimulation during sulfonylurea therapy in **NIDDM**
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Metabolic Research Unit, University of California, San Francisco, CA 94143 United States
Diabetes (DIABETES) (United States) 1986, 35/12 (1314-1320)
CODEN: DIAEA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

Patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) who have chronic hyperglycemia lose acute incremental insulin responses to glucose but are able to briskly reported to other beta-cell secretagogues. To investigate whether this is a defect specific for glucose or represents a more general phenomenon, we measured the insulin responses to acute intravenous tolbutamide in 10 obese patients with **NIDDM** both before

and during sulfonylurea therapy with tolazamide. Comparable glycemia was achieved with oral dextrose 2 h before intravenous testing. To assess beta-cell responsiveness to a nonsulfonylurea secretagogue, 1 mg **glucagon** was **administered** intravenously during tolazamide therapy. In seven patients, the mean peak insulin increment 5 or 10 min after intravenous tolbutamide was 54 +/- 11 muU/ml when not receiving tolazamide (0.14 +/- 1.3 muU/ml) with tolazamide (P < .001), even though serum insulin responded rapidly to intravenous **glucagon**. In four patients tested for reversibility of their refractoriness to intravenous tolbutamide during chronic tolazamide therapy, the mean peak insulin increment 1 wk after discontinuing tolazamide was 79 +/- 22 muU/ml. A relatively rapid development of refractoriness was documented in four patients who were tested only 12 h after beginning tolazamide therapy; the mean peak insulin increments 5-10 min after intravenous tolbutamide were undetectable (-0.5 muU/ml), yet responses to intravenous **glucagon** were evident. In these **NIDDM** patients, exposure of pancreatic beta-cells to sustained levels of sulfonylureas induces a reversible state of refractoriness to acute stimulation with sulfonylureas but not to another secretagogue. This phenomenon has features in common with the effect of sustained hyperglycemia on desensitization of the beta-cell response to intravenous glucose with implications regarding the pathogenesis of **NIDDM**. Moreover, it suggests that the insulinotropic effect of sulfonylureas might be more effective, particularly in cases of **NIDDM** with 'secondary failure' to sulfonylureas, if these drugs are **administered** either on an intermittent schedule or as 'pulse' therapy, using a form with a shorter duration of action.

5/7/122 (Item 35 from file: 73)
DIALOG(R)File 73:EMBASE

03473841 EMBASE No: 1987226422
Glyburide decreases insulin requirement, increases beta-cell response to mixed meal, and does not affect insulin sensitivity: Effects of short- and long-term combined **treatment** in secondary failure to sulfonylurea
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Diabetes Care (DIABETES CARE) (United States) 1987, 10/5 (545-554)
CODEN: DICAD ISSN: 0149-5992
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

In 20 patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) and secondary failure to sulfonylurea, a double-blind randomized study was performed comparing two regimes: insulin plus placebo (IP) and insulin plus glyburide (IG). The protocol included two hospitalization periods (days 1-18 and 78-85) and follow-up at the outpatient clinic for 325 days. The metabolic control was kept as tight as possible. The subjects underwent normoglycemic clamp studies and meal tests with determination of insulin, C-peptide, **glucagon**, somatostatin, and gastric inhibitory polypeptide in plasma. On IG, they demonstrated marked and long-lasting improvement of metabolic control: HbA(1c) decreased from 11.1 +/- 0.3% on day 3 to 8.3 +/- 0.4% (P < .001) on day 78 and 9.1 +/- 0.5% (P < .001) on day 325. In subjects on IP, the corresponding values were 10.3 +/- 0.5, 8.4 +/- 0.4 (P < .001), and 8.9 +/- 0.5% (P < .05). Body weight increased by 6.0 +/- 1.5 kg (P < .005) on IG and 2.9 +/- 2.1 kg (NS) on IP. The daily insulin requirement decreased on IG from 62.5 +/- 12.9 U/day on day 7 to 33.5 +/- 8.8 U/day on day 83 and 34.6 +/- 8.9 U/day on day 325. On IP the insulin requirement was almost constant: 62.0 +/- 10.7 U/day on day 7, 55.5 +/- 7.7 U/day on day 83, and 54.7 +/- 7.9 U/day on day 325. Insulin sensitivity measured with the hyperinsulinemic clamp (plasma

insulin approx. eq.130 muU/ml) was similar on IP and IG at the initiation of the study and was unchanged on days 18 and 85. A key observation of this study, although the mechanism is unclear, is that isoglycemic-meal-related insulin requirement was diminished by insulin **treatment**, indicating improvement of meal-related insulin sensitivity. Glyburide increased basal and meal- but not **glucagon**-stimulated insulin and C-peptide levels, and also augmented the effect of meals on somatostatin release. We conclude that in **NIDDM**, IG regime promptly and continuously decreased insulin requirement and improved metabolic control. This effect is, at least during the first 3 mo, mainly due to enhanced insulin secretion. IG and IP **treatment** had no effect on insulin sensitivity during hyperinsulinemic-normoglycemic clamp, whereas meal-related insulin sensitivity was augmented.

5/7/123 (Item 36 from file: 73)
DIALOG(R)File 73:EMBASE

03469120 EMBASE No: 1987221701

The addition of glipizide to insulin therapy in **Type-II** diabetic patients with secondary failure to sulfonylureas is useful only in the presence of a significant residual insulin secretion

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Acta Endocrinologica (ACTA ENDOCRINOL.) (Denmark) 1987, 116/3 (364-372)
CODEN: ACENA ISSN: 0001-5598
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LANGUAGE: ENGLISH

The present study aimed at 1) investigating the effect of a combined insulin + glipizide **treatment** on the metabolic control (HbA(1c) levels) and insulin requirements (Biostator(R) assessment) in ten non-obese **Type-II** diabetic patients with recent secondary failure to sulfonylureas; and 2) characterizing the relative contributions of changes in endogenous insulin secretion (C-peptide response) and insulin sensitivity (insulin-induced glucose disposal in clamped conditions) to this effect. The patients were **treated** in a randomized cross-over order with either insulin alone or insulin + glipizide (3 x 10 mg/day) during two periods averaging 6 weeks each. Mean HbA(1c) levels were similar in both experimental conditions (8.2 +/- 0.6 vs 7.9 +/- 0.6%, NS). In fact, during the combined therapy, HbA(1c) levels decreased in five subjects (from 8.6 +/- 0.7 to 7.1 +/- 0.5%; 'responders';), but not in the five others ('non-responders'); the 20-h Biostator insulin infusion was significantly decreased in the responders (29%; P <0.05), but not in the non-responders. Basal (0.271 +/- 0.086 vs 0.086 +/- 0.017 nmol/l; P <0.05) and post-**glucagon** (0.468 +/- 0.121 vs 0.180 +/- 0.060 nmol/l; P <0.05) C-peptide plasma levels were significantly higher in the responders than in the non-responders; in addition, glipizide significantly increased basal C-peptide concentrations in the responders only (+ 68%; P <0.05). The insulin-induced glucose disposal was significantly increased by glipizide in the responders (+ 23%; P <0.05), but not in the non-responders; however, this difference could be due to higher plasma free insulin levels (+ 37%; P <0.02) during the clamp with glipizide in the responders who showed persistent C-peptide stimulation. Thus, combining glipizide with insulin seems to be useful only in **Type-II** diabetic patients who still have a significant endogenous insulin secretion capable of being stimulated by this compound.

5/7/124 (Item 37 from file: 73)
DIALOG(R)File 73:EMBASE

03453993 EMBASE No: 1987206570
Pulsatility of insulin and **glucagon** release: Physiological significance and pharmacological implications
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Division of Diabetes, Institute of Medicine, University of Liege, Liege Belgium
Diabetologia (DIABETOLOGIA) (Germany) 1987, 30/7 (443-452)
CODEN: DBTGA ISSN: 0012-186X
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Numerous studies performed in animals (dog, baboon, rhesus monkey) and in man have depicted the existence of peripheral plasma insulin and **glucagon** oscillations. Such oscillations were also reported in the portal blood of dogs and monkeys. The frequency of these oscillations is remarkably stable but their amplitude is increased after a meal and decreased by food deprivation. Sustained oscillations in the release of insulin, **glucagon** and somatostatin from the isolated perfused canine pancreas have been repeatedly reported. Systematic experiments have shown that these oscillations are not affected by exposure to various pharmacological compounds including atropine, propranolol, or dibenziline. The suggestion has been made that the pulsatility of pancreatic hormone release depends on a pacemaker system present in the gland itself. In contrast, conclusive evidence for or against pulsatility of hormone release by isolated islets is still lacking. Similarly, the possible relationship of the slow fluctuations of glucose-induced electrical activity present in certain B cells with pulsatile insulin secretion is still unknown. Several **in vivo** and in vitro studies have shown that pulsatile insulin has greater biological effects than continuous delivery. However, various factors are critical for the demonstration of the superior efficacy of pulsatile insulin; these include duration of hormonal exposure, circulating levels of insulin achieved and, most importantly, coexisting concentrations of circulating **glucagon**. In fact, slight hyperglucagonaemia (in the range of 200 ng-lsup -sup 1) is sufficient to abolish the higher efficacy of pulsatile insulin in man. In vitro studies have shown that pulsatile delivery of **glucagon** is more efficient than continuous exposure to stimulate hepatic glucose protection. Until now, attempts to confirm such effects in man have failed. Finally, recent reports have indicated that pulsatile intravenous insulin infusion in diabetic patients is more efficient than continuous delivery in reducing hepatic glucose production, stimulating glucose utilisation and inhibiting A-cell **glucagon** release. In contrast, attempts to achieve better control of Type 1 **diabetes** by pulsed insulin given subcutaneously have failed. In **Type 2** diabetic patients, preliminary data have shown that the short-term oscillations of plasma insulin are more rapid and generally less regular than in normal subjects; it has been suggested that such disturbances of the normal oscillatory secretory pattern of insulin may contribute to the hyperglucagonaemia of **Type 2 diabetes**.
Until now, attempts to restore normal insulin pulsatility in these patients have failed.

5/7/125 (Item 38 from file: 73)
DIALOG(R)File 73:EMBASE

03416632 EMBASE No: 1987169209
Use of hospital services by elderly diabetics: The Frederica study of

diabetic and fasting hyperglycaemic patients aged 60-74 years
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Diabetic Medicine (DIABETIC MED.) (United Kingdom) 1987, 4/4 (317-321)
CODEN: DIMEE
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

The use of hospital services was studied in 228 patients with known **diabetes** (KD) (52 insulin **treated**, 101 diet plus oral hypoglycaemic agents (OHAs), 66 diet **treated** and 9 without **treatment**) and 87 subjects with fasting hyperglycaemia (FH) found by screening of a well-defined population aged 60-74 years. Ninety per cent were **NIDDM** as evaluated by a high C-peptide response on **glucagon** stimulation. Information about all admissions during the year before ascertainment was obtained from the complete regional computerized hospital registration system. The overall average admission rate per year for KD males was 0.47 and for females 0.50. The average number of bed-days occupied per person-year was 6.8 for KD males and 8.2 for females. These rates are 2-3 times higher than those of the general population. Insulin **treated NIDDM** patients had a rate of 23.9, whereas IDDM patients had a rate of 15.2 bed-days per person-year. The corresponding figures for patients **treated** with OHAs were 3.5 and for patients **treated** with diet 4.6. FH had overall bed-day occupancy rates of 0.50 and 1.09 for males and females, respectively, which was less than half of that expected from the general population. If discharge diagnosis (principal and/or subsidiary) had been used for identification of hospitalized patients with **diabetes** the bed-days used by KD patients would have been underestimated by 15.3%, most pronounced for diabetics **treated** with OHAs (21.1%) or diet (21.6%).

5/7/126 (Item 39 from file: 73)
DIALOG(R)File 73:EMBASE

03383986 EMBASE No: 1987136563
Prevalence of fasting hyperglycemia and known non-insulin-dependent **diabetes** mellitus classified by plasma C-peptide: Fredericia Survey of subjects 60-74 yr old
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Diabetes Care (DIABETES CARE) (United States) 1987, 10/1 (26-32)
CODEN: DICAD
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

A Danish population of 5699 individuals (60-74 yr old) was screened by fasting blood glucose (FBG) and interviewed about known **diabetes**. The distribution of FBG in individuals not known to have **diabetes** showed no sex difference or significant variation with age. Fasting hyperglycemia (FH), defined as FBG >=7 mM in subjects without a history of **diabetes**, was found in 1.7% of men and women. Known **diabetes** (KD) had a prevalence of 3.9 and 5.0% in men and women, respectively. The prevalence rates of FH and KD increased significantly with age. In the two subgroups, plasma C-peptide was measured after overnight fasting and subsequently 6 min after an intravenous injection of **glucagon**. Based on the distribution of the C-peptide concentrations in non-insulin-**treated** KD subjects, lower limits for non-insulin-dependent **diabetes** mellitus (**NIDDM**) of 0.30 pmol/ml for fasting C-peptide and 0.60 pmol/ml for stimulated C-peptide were arbitrarily chosen. According to these cutoff points, only 38.5% of KD subjects **treated** with insulin had

insulin-dependent **diabetes** mellitus, corresponding to 9.3% of all KD subjects. After exclusion of these patients, the prevalence of recognized **NIDDM** was 3.5% in men and 4.5% in women. All FH subjects except one had C-peptide values in the **NIDDM** interval. A clsoe agreement between fasting and **glucagon**-stimulated C-peptide was seen. In epidemiological studies with an expected high prevalence of **NIDDM**, we propose to use fasting C-peptide for classification of patients with insulin-**treated diabetes**.

5/7/127 (Item 40 from file: 73)
DIALOG(R)File 73:EMBASE

03318951 EMBASE No: 1987071528
Combined insulin and sulfonylurea therapy in non-insulin-dependent diabetics with secondary failure to oral drugs: A one year follow-up
Quatraro A.; Consoli G.; Ceriello A.; Giugliano D.
Centro di Diabetologia, Casa di Cura S. Rita, Taranto Italy
Diabete et Metabolisme (DIABETE METABOL.) (France) 1986, 12/6 (315-318)
CODEN: DIMED
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: FRENCH

We studied the influence of chronic sulfonylurea **treatment** on glucose metabolism and beta-cell secretory activity in diabetic patients requiring insulin after secondary failure to oral drugs. Thirty diabetics were allocated at random into two groups, each consisting of 15 subjects: group A continued insulin **treatment**, while group B received combined insulin plus sulfonylurea. Daily doses of the sulfonylurea gliclazide ranged from 40 to 240 mg, and dose adjustment was made on the basis of periodic monthly control. This **treatment** (12 months) caused a significant improvement of both diurnal glucose profile and HbA1 levels; the beta-cell secretory response to 1 mg **glucagon** was significantly increased at the end of the study. There was on average a 40% reduction of the daily insulin dose in the diabetics receiving combined **treatment**. None of these improvements were seen in the control group receiving only insulin for the same period of time. We suggest that combining a sulfonylurea with insulin can be useful in insulin-requiring **type-2** diabetics who still secrete some endogenous insulin.

5/7/128 (Item 41 from file: 73)
DIALOG(R)File 73:EMBASE

03178030 EMBASE No: 1986155607
Islet cell antibodies identify latent type I **diabetes** in patients aged 35-75 years at diagnosis
Groop L.C.; Bottazzo G.F.; Doniach D.
Fourth Department of Medicine, Helsinki University Central Hospital, Helsinki Finland
Diabetes (DIABETES) (United States) 1986, 35/2 (237-241)
CODEN: DIAEA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

One hundred fifty-four selected patients with nonketotic **diabetes** diagnosed between the ages of 35 and 75 yr and **treated** with diet or oral hypoglycemic agents for at least 1 yr were investigated for parameters of glycemic control (weight loss, blood glucose, and glycosylated

hemoglobin), islet cell function (fasting and **glucagon**-stimulated C-peptide responses), and immunologic markers of insulitis (total ICA and CF-ICA) or autoimmunity (thyroid and gastric antibodies). These parameters were all repeated in 9 of 22 ICA-positive patients after a 2-yr follow-up and correlated with secondary drug failure. The antibody tests were also done on 51 nondiabetic controls matched for age and body weight. The 22 (14%) diabetic subjects having positive islet cell antibodies (ICA) included more women than men with a shorter duration of symptoms, lower body weight, more associated thyroid autoimmunity, and a tendency to have more type I **diabetes** in their families, although glycemic control, age at onset, and family history of **type II diabetes** were the same as in the 132 ICA-negative cases. Patients with ICA had lower initial C-peptide levels and showed little rise after **glucagon** stimulation. Beta cell function deteriorated significantly during the 2-yr follow-up in 9 of 22 positive patients and more ICA-positive patients required insulin. It is suggested that these latent type I diabetic patients are characterized by persistent ICA, progressive loss of beta cells, and a high frequency of thyrogastric autoimmunity. The determination of ICA may be of clinical value in the diagnosis and **treatment** of nonketotic **diabetes** with onset in later life.

5/7/129 (Item 42 from file: 73)
DIALOG(R)File 73:EMBASE

03124495 EMBASE No: 1986192072
The 24-hour effects of glyburide and chlorpropamide after chronic **treatment** of **type II** diabetic patients
Prosser P.R.; Kosola J.W.; Bowers C.Y.
Tulane University School of Medicine, Department of Medicine, New Orleans, LA 70112 United States
American Journal of the Medical Sciences (AM. J. MED. SCI.) (United States) 1985, 289/5 (179-185)
CODEN: AJMSA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

A single-blind, randomized, comparative evaluation of glyburide (GL) and chlorpropamide (CP) therapy was performed in 20 previously untreated patients with non-insulin dependent **diabetes** mellitus (**NIDDM**) of about 2 years' duration. Only newly diagnosed patients who were never **treated** and whose fasting blood glucose (FBS) levels were >140 mg/dl after a 6- to 8-week trial of dietary restriction were evaluated. Metabolic studies were performed before and after 4 months of therapy. GL and CP produced essentially the same effects on serum levels of glucose, insulin, **glucagon** (IRG), growth hormone (GH), cholesterol, and triglyceride. The mean 24-hour glucose levels for both the GL and CP groups were significantly lower than the pretherapy values ($p < 0.001$). The mean 24-hour insulin levels did not change significantly during therapy ($p > 0.05$). Excellent control of plasma glucose was possible during the entire day without producing nocturnal hypoglycemia. Neither GL nor CP therapy influenced the mean 24-hour levels of IRG, GH, or cholesterol. However, mean 24-hour levels of triglyceride were lower in both groups. IRG levels were elevated and the pattern of change in the insulin and IRG levels paralleled each other, which suggested that **glucagon** may play a role in the resistance of insulin action in **NIDDM**. GH levels were normal and remained unchanged during therapy. It was concluded that detailed 24-hour studies are important for better understanding the spectrum of abnormalities in newly diagnosed patients with **NIDDM** who were never **treated**. Results of the glucose-insulin interrelationships throughout the day and night indicate that these **NIDDM** patients appear to have

an islet cell impaired glucose/insulin release abnormality as well as a resistance to the action of insulin. Chronic therapy with GL or CP appeared to lower glucose levels by improving insulin action.

5/7/130 (Item 43 from file: 73)
DIALOG(R)File 73:EMBASE

03117388 EMBASE No: 1986184965
Prevalence of insulin deficiency among initially non-insulin-dependent middle-aged diabetic individuals
Laakso M.; Sarlund H.; Pyorala K.
Department of Medicine, Kuopio University Central Hospital, 70210 Kuopio 21 Finland
Diabetes Care (DIABETES CARE) (United States) 1986, 9/3 (228-231)
CODEN: DICAD
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

The endogenous insulin secretion capacity of 171 insulin-**treated** middle-aged persons with **diabetes** (81 men, 90 women) of the Kuopio University Central Hospital district (population 250,000), East Finland, was measured by the C-peptide response to **glucagon**. The prevalence of insulin deficiency among initially non-insulin-dependent diabetic (**NIDDM**) individuals was calculated on the basis of those who were initially **treated** with diet or oral drugs and 3 yr or more after diagnosis had been **treated** with insulin and were insulin deficient in this study. The prevalence of complete insulin deficiency (postglucagon C-peptide undetectable) was among initially **NIDDM** individuals of the same region, 0.7% in men and 1.2% in women. Using the postglucagon C-peptide level of 0.20 nmol/L as a cut-off point, the prevalence of insulin deficiency was 2.0% in men and 1.9% in women and, on the basis of C-peptide level of 0.60 nmol/L, the prevalence of insulin deficiency was 3.5% in men and 2.7% in women. Our data suggest that the deterioration of insulin secretion capacity in **NIDDM** to the level that leads to insulin dependency occurs less often than has been previously suggested.

5/7/131 (Item 44 from file: 73)
DIALOG(R)File 73:EMBASE

03038017 EMBASE No: 1985231533
Pharmacokinetics and metabolic effects of glibenclamide and glipizide in **type 2** diabetics
Groop L.; Wahlin-Boll E.; Groop P.-H.; et al.
Third and Fourth Medical Departments of Medicine, University of Helsinki, Helsinki Finland
European Journal of Clinical Pharmacology (EUR. J. CLIN. PHARMACOL.) (Germany) 1985, 28/6 (697-704)
CODEN: EJCPA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

Fifteen **Type 2** diabetics were **treated** for 4-week periods with once daily (10 mg) glibenclamide, glipizide and placebo according to a double-blind cross-over protocol. Post-dose glipizide concentrations were three times higher than those of glibenclamide, due to the incomplete bioavailability of the latter. On the other hand, pre-dose drug level were similar, as an expression of the slower absorption and/or elimination of glibenclamide. Both active **treatments** reduced

postprandial blood glucose concentrations and 24-hour urinary glucose excretion to a similar degree, but fasting blood glucose concentrations were slightly lower during glibenclamide **treatment**. Both active **treatments** enhanced fasting and postprandial insulin and C-peptide concentrations, the C-peptide response being greater after glipizide than after glibenclamide. Plasma **glucagon** and GIP concentrations were not significantly affected. Insulin sensitivity was increased by glibenclamide but not by glipizide. Neither therapy affected insulin binding to erythrocytes. It appears that both glibenclamide and glipizide improved glucose metabolism by sustained stimulation of insulin secretion, which was most pronounced with glipizide. Only glibenclamide improved insulin sensitivity and was slightly more active than glipizide on fasting blood glucose levels. The differences may be consequences of the pharmacokinetics, but differences in pharmacodynamics cannot be excluded.

5/7/132 (Item 45 from file: 73)
DIALOG(R)File 73:EMBASE

03014828 EMBASE No: 1985008794
Treatment of **type II diabetes**
CONSIDERATIONS SUR LE TRAITEMENT DU DIABETE DE **TYPE II**
Berger W.; Pasquel M.
Abteilung fur Endokrinologie und Stoffwechsel, Medizinische Universitatsklinik, Kantonsspital Basel, 4031 Basel Switzerland
Medecine et Hygiene (MED. HYG.) (Switzerland) 1984, 42/1580 (3162-3172)
CODEN: MEHGA
DOCUMENT TYPE: Journal
LANGUAGE: FRENCH

5/7/133 (Item 46 from file: 73)
DIALOG(R)File 73:EMBASE

03010625 EMBASE No: 1985004591
Glucose counterregulation in patients after pancreatectomy. Comparison with other clinical forms of **diabetes**
Polonsky K.S.; Herold K.C.; Gilden J.L.; et al.
Department of Medicine, University of Chicago, Pritzker School of Medicine, Chicago, IL United States
Diabetes (DIABETES) (United States) 1984, 33/11 (1112-1119)
CODEN: DIAEA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

Glucose and counterregulation hormone responses to a high-dose (1.7 mU/kg/min) insulin infusion were studied in 6 patients who had undergone total pancreatectomy, and the results were compared with those of normal controls and patients with other clinical forms of **diabetes**. The maximum increase in the plasma **glucagon** concentration during hypoglycemia in the pancreatectomized patients (5 +/- 5.6 pg/ml) was less than in normals (121 +/- 22 pg/ml). Type I diabetic subjects (28 +/- 14 pg/ml), and insulin-**treated** diabetic subjects of recent onset (36 +/- 12 pg/ml) also had reduced responses, while responses were normal in **type II** diabetic subjects (102 +/- 26 pg/ml). The epinephrine response to the hypoglycemic stimulus was reduced after pancreatectomy (278 +/- 81 pg/ml) and in type I diabetic subjects (628 +/- 244 pg/ml), but was not different from control (858 +/- 126 pg/ml) in **type II** and recent-onset diabetic patients. There was considerable overlap in

counterregulation hormone responses in individual patients with and without autonomic neuropathy and with normal or undetectable fasting C-peptide concentrations. While the control subjects all experienced symptoms of hypoglycemia within a narrow range of plasma glucose concentrations (35-46 mg/dl), five of the diabetic subjects experienced symptoms of hypoglycemia at plasma glucose levels of >=55 mg/dl, and five had no subjective awareness of hypoglycemia despite plasma glucose levels <30 mg/dl. Thus, (1) after pancreatectomy both **glucagon** and epinephrine responses are reduced, resulting in markedly impaired glycose recovery from insulin-induced hypoglycemia; (2) **glucagon** responses may be abnormal in insulin-**treated** diabetic subjects within the first year of diagnosis, despite relatively normal fasting C-peptide concentrations and no clinical evidence of autonomic neuropathy; and (3) **glucagon** and epinephrine responses are normal in **type II** diabetic subjects even if the disease is of prolonged duration and clinical evidence of autonomic neuropathy is present.

5/7/134 (Item 47 from file: 73)
DIALOG(R)File 73:EMBASE

02983631 EMBASE No: 1985027592
Effect of sodium salicylate on hormonal responses to hypoglycaemia in **type II** diabetics
Brass E.P.; Halter J.B.; Ensinck J.W.; Robertson R.P.
Department of Medicine, University of Colorado Health Sciences Center, Denver, CO 80262 United States
Clinical Endocrinology (CLIN. ENDOCRINOL.) (United Kingdom) 1984, 21/6 (649-655)
CODEN: CLENA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

Prostaglandins and prostaglandin synthesis inhibitors are known to influence the secretion of a number of hormones. More specifically, sodium salicylate is known to increase insulin secretion in **Type II** diabetics in response to a glucose stimulus. To challenge the hypothesis that prostaglandins may be instrumental in a generalized defect of glucose recognition in **Type II** diabetics, the effect of sodium salicylate on the hormonal counter-regulatory response to insulin-induced hypoglycaemia was examined. Before salicylate **treatment**, seven **Type II** diabetics had brisk increases (mean +/- SEM) in circulating adrenaline (time 0 = 50 +/- 7 pg/ml; peak = 1630 +/- 330 pg/ml), noradrenaline (time 0 = 260 +/- 46 pg/ml; peak = 770 +/- 140 pg/ml), **glucagon** (time 0 = 38 +/- 6 pg/ml; peak = 75 +/- 10 pg/ml) and pancreatic polypeptide (time 0 = 149 +/- 30 pg/ml; peak = 1170 +/- 180 pg/ml) in response to insulin-induced hypoglycaemia. In contrast to previous studies in normal subjects, **treatment** with sodium salicylate failed to augment hypoglycaemia-induced secretion of adrenaline, noradrenaline or pancreatic polypeptide in **Type II** diabetics. The **glucagon** response to hypoglycaemia was augmented by sodium salicylate when the data were expressed as the incremental area under the **glucagon** vs. time curve, but not when peak response was used for analysis. These results are inconsistent with a prostaglandin-related generalized defect in glucose recognition in **Type II** diabetics and suggest that augmentation of hormone secretion in these patients by sodium salicylate may be specific for glucose-induced insulin secretion.

5/7/135 (Item 48 from file: 73)
DIALOG(R)File 73:EMBASE

02940820 EMBASE No: 1985084779
The effect of insulin **treatment** on insulin secretion and insulin action in **type II diabetes** mellitus
Garvey W.T.; Olefsky J.M.; Griffin J.; et al.
Division of Endocrinology and Metabolism, Department of Medicine, University of California, San Diego, CA United States
Diabetes (DIABETES) (United States) 1985, 34/3 (222-234)
CODEN: DIAEA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

We have studied the effects of 3 wk of continuous subcutaneous insulin infusion (CSII) on endogenous insulin secretion and action in a group of 14 **type II** diabetic subjects with a mean (+/-SEM) fasting glucose level of 286 +/- 17 mg/dl. Normal basal and postprandial glucose levels were achieved during insulin therapy at the expense of marked peripheral hypserinsulinemia. During the week of posttreatment evaluation, the subjects maintained a mean fasting glucose level of 155 +/- 11 mg/dl off insulin therapy, indicating a persistent improvement in carbohydrate homeostasis. Adipocyte insulin binding and **in vivo** insulin dose-response curves for glucose disposal using the euglycemic clamp technique were measured before and after therapy to assess the effect on receptor and post-receptor insulin action. Adipocyte insulin binding did not change. The insulin dose-response curve for overall glucose disposal remained right-shifted compared with age-matched controls, but the mean maximal glucose disposal rate increased by 74% from 160 +/- 14 to 278 +/- 18 mg/msup 2/min ($P < 0.0005$). The effect of insulin **treatment** on basal hepatic glucose output was also assessed; the mean rate was initially elevated at 159 +/- 8 mg/msup 2/min but fell to 90 +/- 5 mg/msup 2/min in the posttreatment period ($P < 0.001$), a value similar to that in control subjects. Endogenous insulin secretion was assessed in detail and found to be improved after exogenous insulin therapy. Mean 24-h integrated serum insulin and C-peptide concentrations were increased from 21.377 +/- 2766 to 35.584 +/- 4549 muU/ml/min ($P < 0.01$) and from 1653 +/- 215 to 2112 +/- 188 pmol/ml/min ($P < 0.05$), respectively, despite lower glycemia. Second-phase insulin response to an intravenous (i.v.) glucose challenge was enhanced from 170 +/- 53 to 1022 +/- 376 muU/ml/min ($P < 0.025$), although first-phase response remained minimal. Finally, the mean insulin and C-peptide responses to an i.v. **glucagon** pulse were unchanged in the posttreatment period, but when glucose levels were increased by exogenous glucose infusion to approximate the levels observed before therapy and the **glucagon** pulse repeated, responses were markedly enhanced. Simple and multivariate correlation analysis showed that only measures of basal hepatic glucose output and the magnitude of the postbinding defect in the untreated state could be related to the respective fasting glucose levels in individual subjects. We conclude that after 3 wk of intensive insulin therapy, diabetic subjects maintain lower glucose values concomitant with: (1) partial reversal of the postbinding defect in peripheral insulin action, (2) near-normalization of basal hepatic glucose output, and (3) enhanced insulin secretory responses. First-phase insulin response remained minimal and may be a marker for the diabetic state. Correlation analysis could only implicate basal hepatic glucose output and the postbinding defect in the untreated state as direct determinants of the fasting glucose level.

5/7/136 (Item 49 from file: 73)
DIALOG(R)File 73:EMBASE

02934959 EMBASE No: 1985078918
Transient effect of the combination of insulin and sulfonylurea (glibenclamide) on glycemic control in non-insulin dependent diabetics poorly controlled with insulin alone
Groop L.; Harno K.; Nikkila E.A.; et al.
Third Department of Medicine, Helsinki University Central Hospital, Helsinki Finland
Acta Medica Scandinavica (ACTA MED. SCAND.) (Sweden) 1985, 217/1 (33-39)
CODEN: AMSVA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

In a double-blind cross-over study we compared the effects of insulin plus glibenclamide, 5 mg twice daily, with insulin plus placebo during 8-week periods on metabolic parameters in 13 non-insulin dependent diabetic (**NIDDM**) patients poorly controlled with insulin alone. The combination therapy improved diabetic control as assessed by fasting blood glucose ($p < 0.001$), 24-hour urinary glucose ($p < 0.01$) and glycohemoglobin (HbAinf 1) concentrations ($p < 0.05$ at week 12). The effect tended to cease with time. Significantly higher C-peptide values were found during combination **treatment** than during insulin-placebo ($p < 0.01$) and the changes in fasting C-peptide concentrations correlated positively with the changes in HbAinf 1 concentrations ($r = 0.56$, $p < 0.05$). There was no difference in **glucagon** concentrations, insulin binding to erythrocytes or insulin sensitivity between the two study periods. Neither did the combination therapy influence blood lipids significantly. The present study shows that the combination of insulin and glibenclamide may be of limited value in the **treatment** of **NIDDM** patients poorly controlled with insulin alone. However, thus far the long-term results are uncertain. In the absence of significant effects on insulin binding and insulin sensitivity, the improved diabetic control seems to be explained, at least partly, by glibenclamide-induced stimulation of insulin secretion.

5/7/137 (Item 50 from file: 73)
DIALOG(R)File 73:EMBASE

02878642 EMBASE No: 1985172601
Influence of calcium-antagonists on pancreatic endocrine secretion
INFLUENZA DEI FARMACI CALCIO-ANTAGONISTI SULLA SECREZIONE EENDOCRINA PANCREATICA
Vincenzi V.; Fioroni E.; Benvegnu B.; et al.
Universita di Perugia, c/o Ospedale Civile S. Maria, Terni Italy
Minerva Medica (MINERVA MED.) (Italy) 1985, 76/19-20 (919-921)
CODEN: MIMEA
DOCUMENT TYPE: Journal
LANGUAGE: ITALIAN SUMMARY LANGUAGE: ENGLISH

The influence of verapamil, a calcium antagonist, on circulating levels of glucose, insulin and **glucagon** has been evaluated in 5 normal subjects and in 5 patients with non insulin-dependent **diabetes** (**NIDDM**). An oral glucose tolerance test was performed both in basal conditions and during intravenous infusion of the drug (5 mg/h). Administration of Verapamil didn't induce any significant change on the three parameters. The small decrease of glicemia in patients affected by **NIDDM** and **treated** with Verapamil was not related to reduction of glucagonemia.

5/7/138 (Item 51 from file: 73)

DIALOG(R)File 73:EMBASE

02848148 EMBASE No: 1985192107
Abnormal insulin secretion in a streptozocin model of **diabetes**: Effects of insulin **treatment**
Leahy J.L.; Bonner-Weir S.; Weir G.C.
Division of Endocrinology, Department of Internal Medicine, Medical College of Virginia, Richmond, VA United States
Diabetes (DIABETES) (United States) 1985, 34/7 (660-666)
CODEN: DIAEA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

We have proposed that chronic hyperglycemia causes the abnormal glucose influence on arginine-stimulated insulin secretion in the neonatal streptozocin (STZ) rat model of **NIDDM** and therefore studied the effect of 24 h of mild insulin-induced hypoglycemia on this defect. Ultralente insulin, 20 U/kg, was given at 9 a.m. and 10 U/kg at 5 p.m., and insulin and **glucagon** secretion were then studied the next morning using the in vitro isolated, perfused pancreas. The fed plasma glucose concentrations decreased in the STZ rats from 191 +/- 13 to 101 +/- 9 mg/dl and from 133 +/- 4 to 99 +/- 8 mg/dl in the controls. As expected, 10 mM arginine caused a trivial insulin response at 2.8 mM glucose in the **treated** and untreated control groups compared with the marked one at 16.7 mM. The response to arginine at 2.8 mM glucose in the untreated STZ rats, however, was strikingly elevated (7.65 +/- 2.29 versus 0.41 +/- 0.16 ng/ml in the untreated controls) and it was not potentiated by the high glucose background, but the result at 2.8 mM glucose in the **treated** STZ rats was similar to that of the **treated** controls (0.46 +/- 0.12 versus 0.16 +/- 0.03 ng/ml). A return of glucose influence on IBMX-stimulated insulin secretion was also noted. Glucose-induced insulin release, however, was not restored in the **treated** STZ rats, but it was markedly suppressed in the controls by the insulin **treatment**. Glucose influence on the **glucagon** response to arginine was maintained in the STZ model even though the **glucagon** release to a lowered glucose concentration was lost. These data suggest that chronic hyperglycemia causes the abnormal glucose influence on arginine-stimulated insulin release in the STZ model of **diabetes**.

5/7/139 (Item 52 from file: 73)
DIALOG(R)File 73:EMBASE

02781113 EMBASE No: 1984000072
Counterregulatory hormone release and glucose recovery after hypoglycemia in non-insulin-dependent diabetic patients
Boden G.; Soriano M.; Hoeldtke R.D.; Owen O.E.
Department of Medicine, Division of Metabolism/Diabetes, Temple University Health Sciences Center, Philadelphia, PA United States
Diabetes (DIABETES) (United States) 1983, 32/11 (1055-1059)
CODEN: DIAEA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

An increasing number of patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) is presently being **treated** with insulin, some aggressively with intensified **treatment** schedules. However, there is little information on the ability of these patients to recover from insulin-induced hypoglycemia. We have, therefore, determined glucose recovery and counterregulatory hormone secretion in response to

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...examined 50 records  (850)
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glucose-stimulated insulin output from the beta cell. We aimed at finding out whether this characteristic disorder is a consequence of reduced beta cell mass or of a more functional disturbance. In the latter case it was to be clarified whether the disturbed beta cell 'glucoreceptor' function represents a qualitative or rather a quantitative difference. By the evaluation of insulin secretion and of carbohydrate tolerance during oral and/or intravenous intake of glucose, and after intravenous application of tolbutamide or **glucagon** the defective insulin secretion in **type II** diabetics was found to represent a more functional disturbance which could not be explained by reduction of beta cell mass. Thus it was concluded that the anomaly of insulin secretion mentioned above might be a consequence of a qualitative defect of the glucoreceptor. To prove this, isolated human islets (insulin secretion under incubation with glucose, measurements of sup 3H-leucine incorporation and of the insulin content) were also studied. In contrast to the **in vivo** results, insulin release of the isolated islets of **type II** diabetics was normal. From this it must be concluded that the glucoreceptor of the beta cell, which **in vivo** reacts in a qualitatively different manner from that of subjects with intact metabolism, is not irreversibly disturbed. These discrepancies between the **in vivo** and in vitro results could possibly be explained by the existence of circulating or of intrapancreatic antagonists of glucose action on insulin secretion or by an increased responsiveness of the islets of diabetics to normal concentrations of inhibiting substances.

5/7/142 (Item 55 from file: 73)
DIALOG(R)File 73:EMBASE

02693726 EMBASE No: 1984112685
Influence of verapamil on glucose tolerance
Rojdmark S.; Andersson D.E.H.
Department of Internal Medicine II, Sodersjukhuset, 100 64 Stockholm 38 Sweden
Acta Medica Scandinavica (ACTA MED. SCAND.) (Sweden) 1984, 215/SUPPL. 681 (37-42)
CODEN: AMSVA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

Verapamil has previously been found to inhibit insulin release from pancreatic beta-cells in laboratory animals. In our department, however, both oral pretreatment with verapamil for one week and a 3-hour iv infusion of the drug improved the tolerance to oral glucose in **type II** diabetics without affecting insulin release. It failed, however, to potentiate the hypoglycaemic effect of oral glibenclamide therapy in patients with **type II diabetes**. Since iv infusion of verapamil left the portal vein glucose response to glucose ingestion in normoglycaemic patients (being portal vein catheterised for diagnostic purposes), it seems unlikely that the hypoglycaemic effect of verapamil could have been due to reduced glucose absorption from the gut. More likely is that verapamil, in the diabetic patients, influenced metabolic processes inside the hepatocytes that are of importance for insulin homeostasis. In-vitro experiments have shown that calcium affects factors of importance for the glucose metabolism. Accordingly, calcium triggers the stimulus-secretion coupling process which leads to insulin release from the pancreatic beta-cells. Calcium also tightens cell membranes, thereby decreasing their permeability to various substances, including glucose. Finally, calcium mediates cellular responses to **glucagon** stimulation and thus affects the hepatic glucose output. Calcium apparently influences glucose metabolism by several pathways and different overall effects on the

blood glucose concentration may be forthcoming depending on which of these pathways is the dominating one. In view of these well-documented in-vitro effects of calcium on some of the metabolic processes which determine the glucose tolerance, it is surprising to find that relatively few clinical studies have been carried out to investigate whether calcium antagonists influence glucose tolerance in man. Although a few such studies, dealing with the effect of nifedipine and verapamil on human glucose tolerance have been performed recently, the result obtained in these investigations have been highly conflicting. Our intention has therefore been to elucidate how oral and iv administration of verapamil affects glucose tolerance not only in normoglycaemic subjects, but also in patients with untreated, and sulfonylurea-**treated type II diabetes**.

5/7/143 (Item 56 from file: 73)
DIALOG(R)File 73:EMBASE

02637665 EMBASE No: 1984156623
Acute and chronic effects of sulfonylurea drugs on pancreatic islet function in man
Pfeifer M.A.; Halter J.B.; Judzewitsch R.G.; et al.
Veterans Administration Medical Centers, Seattle, WA United States
Diabetes Care (DIABETES CARE) (United States) 1984, 7/SUPPL. 1 (25-34)
CODEN: DICAD
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

The pancreatic islet can be viewed as an integrator of nutrient, neural, and hormonal signals. In normal people, glucose directly stimulates insulin release and also plays a key role as a potentiator of nonglucose stimulants of the B-cells. In patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**), the direct effect of glucose on insulin secretion is markedly impaired. However, as hyperglycemia develops, basal insulin levels and insulin responses to nonglucose signals are maintained in many NIDD patients by the potentiating effect of hyperglycemia. Both acute and chronic administration of sulfonylurea drugs results in enhanced B-cell sensitivity to the potentiating effect of glucose. During sulfonylurea therapy this effect initially causes an increase in insulin level. However, as the glucose level falls during therapy the insulin level may tend to return toward pretreatment values, thereby masking the improvement of B-cell function. In NIDD patients with mild to moderate hyperglycemia (fasting plasma glucose <200 mg/dl), chronic sulfonylurea therapy results in the maintenance of near-normal insulin levels, but at a lower plasma glucose level. In patients with more severely impaired B-cell function, whose insulin levels before therapy are subnormal despite marked hyperglycemia, there is a net absolute increase in insulin levels during chronic sulfonylurea administration. Thus, some NIDD patients may show an increase in basal insulin levels during chronic sulfonylurea therapy while others may not; however, all patients who respond to sulfonylureas demonstrate increased B-cell sensitivity to glucose. Acute and chronic sulfonylurea **treatment** also results in a suppression of **glucagon** levels, an effect that may be secondary to the enhancement of B-cell function. The fall of plasma glucose during chronic sulfonylurea therapy is associated with a decrease in hepatic glucose production in NIDD patients. The magnitude of this effect is correlated with the degree of enhancement of basal insulin secretion. Thus, chronic sulfonylurea therapy clearly enhances pancreatic islet function in patients with **NIDDM**. We postulate that the major antihyperglycemic action of sulfonylurea therapy is mediated by this pancreatic effect.

5/7/144 (Item 57 from file: 73)
DIALOG(R)File 73:EMBASE

02540859 EMBASE No: 1983014870
C-peptide reactivity as a measure of insulin dependency in obese diabetic patients **treated** with insulin
Hoekstra J.B.L.; Van Rijn H.J.M.; Thijssen J.H.H.; Erkelens D.W.
Dep. Int. Med., Univ. Hosp., 3511 GV Utrecht Netherlands
Diabetes Care (DIABETES CARE) (United States) 1982, 5/6 (585-591)
CODEN: DICAD
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

The C-peptide increase after an oral glucose tolerance test (OGTT) and intravenous **glucagon** test (GT) was assessed to establish actual insulin dependency in 16 obese diabetic patients **treated** with insulin for years. The results, compared to five reference groups, showed two types of reaction: first, a negative response in 3 patients with a minimal C-peptide increase after either stimulation (range 0-0.1 ng/ml during GT, 0-0.5 during OGTT), not different from that in the insulin-dependent reference group (GT: 0.1 +/- 0.2, OGTT: 0.1 +/- 0.3 x- +/- SD). Second, a positive response in 13 patients with a C-peptide increase, different from that in the insulin-dependent group after **glucagon** (range 0.7-5.6), and in 6 patients after OGTT (range 0.8-1.8). When insulin **treatment** was discontinued in two nonresponders, the B-hydroxybutyrate levels and ketobutyrate levels increased to over 2.1 and 0.60 mmol/L within 10 days, proving insulin dependency, and thus type I **diabetes**. B-hydroxybutyrate and ketobutyrate levels increased to maximal 0.4 and 0.17 after stopping insulin therapy in nine positive responders. No ketoacidosis developed during a 4-wk follow-up, indicating non-insulin dependency (**type II diabetes**). Measuring C-peptide after **glucagon** is a simple test that may be a discriminative method to establish insulin dependency in obese diabetic patients **treated** with insulin.

5/7/145 (Item 58 from file: 73)
DIALOG(R)File 73:EMBASE

02325381 EMBASE No: 1983204385
Exercise and **diabetes** mellitus: Physical activity as a part of daily life and its role in the **treatment** of diabetic patients
Kemmer F.W.; Berger M.
Med. Klin. E, Univ. Dusseldorf, D-4000 Dusseldorf Germany
International Journal of Sports Medicine (INT. J. SPORTS MED.) (Germany) 1983, 4/2 (77-88)
CODEN: IJSMD
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

In normal man, glucose homeostasis and adequate fuel supply to the working muscle and other vital organs is maintained due to a finely tuned interplay of hormonal regulation by insulin, catecholamines, **glucagon** , cortisol, and growth hormone. In type I **diabetes** mellitus, physiologic glucoregulation is offset because of endogenous insulin deficiency and unphysiologic insulin substitution by subcutaneous injections. As various states of insulin deficiency or surplus may occur in these patients, exercise can either increase glycemia and possibly lead to severe ketoacidosis or reduce blood glucose levels and under certain conditions precipitate hypoglycemia. The role of exercise as a therapeutic

measure for improving metabolic control that had been advocated during the early insulin aera is not supported by experimental evidence. In contrast, the rather large body of information about physiologic and pathophysiologic mechanisms in glucoregulation indicates that such a therapeutic role of exercise cannot be put into practice because the glycemic reactions to exercise depend on too many inter- and intraindividual variables, such as state of nutrition, training and metabolic control, intensity, duration, and time of exercise performance. On the other hand, all type I diabetics should be strongly motivated to exercise whenever they want to in order to maintain their physical fitness and for recreational purposes. To prevent hypoglycemia, the predominant hazard of exercise in **diabetes**, the patients have to be instructed by means of specific programs of **diabetes** education to take certain preventive measures, such as dose reduction of insulin and increments of carbohydrate intake in association with the physical activity. While in type I **diabetes** mellitus physical exercise has no practical importance as a therapeutic measure, permanent increase in physical activity must be considered a most important measure in the therapy of **type II diabetes** mellitus because physical training has been shown to reduce cardiovascular risk factors and is likely to improve peripheral insulin resistance, which is a central feature of **type II diabetes** mellitus.

5/7/146 (Item 59 from file: 73)
DIALOG(R)File 73:EMBASE

02311076 EMBASE No: 1983242237
A stimulatory effect of tolbutamide on the insulin-mediated glucose uptake in subjects with impaired glucose tolerance (IGT)
Schulz B.; Ratzmann K.P.; Heinke P.; Besch W.
Cent. Inst. Diabetes Gerhardt Katsch, Karlsburg GDR-2201 Germany
Experimental and Clinical Endocrinology (EXP. CLIN. ENDOCRINOL.) (Germany) 1983, 82/2 (222-231)
CODEN: EXCED
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

Several studies have indicated that the long-term effectiveness of sulfonylurea therapy in the **treatment** of **type-II** diabetics is due to a potentiation of insulin action. The present investigation was undertaken in order to elucidate whether or not there is also an acute effect of sulfonylureas on insulin-mediated glucose uptake. Nine non-obese subjects classified as having impaired glucose tolerance formed the study group. **In vivo** insulin sensitivity was assessed by using the glucose controlled insulin infusion system (Biostator(R)) without or with a contemporary 3-hour tolbutamide infusion. Studies were performed on subsequent days, and each subject served as its own control. Glucose was given at a fixed rate of 0.011 mmol/kg b.w./min. The computer program was set to maintain plasma glucose concentration at 3.89 mmol/l. The amount of exogenous insulin necessary to keep glycemia at this steady-state level has been accepted as an estimate of insulin sensitivity. Mean plasma glucose and insulin concentrations were constant and comparable in control and sulfonylurea **treated** groups. Under our experimental conditions tolbutamide did not provoke any increase of C-peptide secretion. There was no significant alteration of insulin counterregulatory hormones (**glucagon** and growth hormone) either. On the other hand, for the disposal of identical quantities of glucose the necessary amount of insulin has been found to be reduced by one third due to tolbutamide **treatment** indicating a higher insulin sensitivity. The mechanism by which tolbutamide intensifies the insulin effect is unknown. It seems to be that a successful short-term sulfonylurea therapy on glucose

utilization is associated with some alterations on the receptor and/or post-receptor level.

5/7/147 (Item 60 from file: 73)
DIALOG(R)File 73:EMBASE

01874896 EMBASE No: 1981182055
The effect of **treatment** of **type 2** (insulin independentj) **diabetes** mellitus on plasma concentrations of pancreatic polypeptide and **glucagon**
Berger D.; Floyd Jr. J.C.; Pek S.B.
Dept. Int. Med., Univ. Michigan, Ann Arbor, Mich. 48109 United States
Diabetologia (DIABETOLOGIA) (Germany) 1981, 21/2 (120-125)
CODEN: DBTGA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

The effect of the control of **diabetes** with diet and insulin upon plasma levels of human pancreatic polypeptide and **glucagon** was determined in eight patients with **Type 2** (insulin independent) **diabetes** mellitus. The mean +/- SEM fasting plasma glucose was 15.9 +/- 1.3 mmol/l for 5 days of diet **treatment** and 5.9 +/- 0.4 mmol/l for the last 5 days of **treatment** with diet plus insulin ($p < 0.0001$); corresponding fasting plasma pancreatic polypeptide levels were 328 +/- 97 and 247 +/- 71 pg/ml ($p < 0.05$) and immunoreactive **glucagon** levels were 95 +/- 11 and 62 +/- 6 pg/ml ($p < 0.005$). Cooked ground beef was **administered** on the first day of diet **treatment** and on the last day of **treatment** with diet plus insulin; mean maximal rise of pancreatic polypeptide, and total and incremental plasma pancreatic polypeptide response areas were significantly lower following **treatment** ($p < 0.01$), as was total area for immunoreactive **glucagon** ($p < 0.05$). Normalisation of fasting plasma glucose by short-term **treatment** with diet plus insulin is associated with decreases in basal and stimulated secretory activity of the pancreatic polypeptide cells in insulin independent **diabetes** mellitus.

5/7/148 (Item 61 from file: 73)
DIALOG(R)File 73:EMBASE

01624408 EMBASE No: 1980182083
Autoantibodies to duodenal gastric-inhibitory-peptide (GIP) cells and to secretin (S) cells in patients with coeliac disease, tropical sprue and maturity-onset **diabetes**
Mirakian R.; Bottazzo G.F.; Doniach D.
Dept. Immunol., Arther Stanley House, Middlesex Hosp. Med. Sch., London W1P 9PG United Kingdom
Clinical and Experimental Immunology (CLIN. EXP. IMMUNOL.) (United Kingdom) 1980, 41/1 (33-42)
CODEN: CEXIA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

The presence of autoantibodies detected by immunofluorescence to single endocrine cells of human duodenum is described in three groups of patients and two control groups. Of 173 coeliac cases, four had GIP cell antibodies, one had secretin cell antibodies and twenty-one reacted with both cell types. Of twelve tropical sprue sera, four reacted with the same two cells. Among fifty elderly diabetics **treated** with hypoglycaemic drugs, seven

sera gave a positive cytoplasmic IFL on duodenal substrate. Four were identified as GIP cells by use of the appropriate hormone antiserum and three reactions were against cells distinct from those stained by anti-GIP, -secretin, -somatostatin, -**glucagon** and -gastrin. Additional gut hormone antisera will have to be tested to identify these APUD cells. Thirty blood donors and seventy-three sera from autoimmune endocrine patients gave entirely negative results on unfixed cryostat sections of duodenal mucosa. Although impaired GIP and secretin responses have been reported in coeliac disease, and abnormal GIP values were found in **Type II diabetes**, there is as yet no data to correlate these metabolic deficiencies with the presence of endocrine cell antibodies in the serum. These studies are in progress.

5/7/149 (Item 1 from file: 94)
DIALOG(R)File 94:JICST-EPlus

01726638 JICST ACCESSION NUMBER: 93A0124372 FILE SEGMENT: JICST-E
Clssification of **Diabetes** in Patients between IDDM and **NIDDM** by Discriminant Function Analysis.
NAGAYOSHI MICHIKO (1); HIGA KIYONORI (1); MURAKAMI KEIJI (1); MIMURA GORO (1)
(1) Univ. of Ryukyus, School of Medicine
Ryukyu Igakkaishi(Ryukyu Medical Journal), **1992**, VOL.12,NO.3, PAGE.244-252, FIG.3, TBL.4, REF.21
JOURNAL NUMBER: Y0266ACI ISSN NO: 0289-1530
UNIVERSAL DECIMAL CLASSIFICATION: 616.39-07
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: It is very difficult to determine the type of **diabetes** in patients after they have been **treated** with insulin. In order to classify **diabetes** in such patients, clinical manifestations and pancreatic B cell function together with the immunogenetic factors of **diabetes** were studied. Utilizing WHO criteria, 78 subjects were divided into three groups IDDM (33), **NIDDM** (19) and unclassified (26). The clinical manifestations at the age of their onset, family history of **diabetes**, **glucagon** stimulated peak plasma C-peptide (P-CPR), insulin dose and HLA type (DR4, DR9, DR2) were studied. These indicators were used as discriminatory variables for classifying **diabetes** in the Forward Selection Discriminant Function Analysis of IDDM and **NIDDM**. Among these variables, P-CPR (X1), age at onset (X2), HLA DR4 (X3) and a family history of **diabetes** (X4) were selected as effective discriminatory variables, and the discriminant coefficients appeared in order of importance. The linear discriminant function was expresed as Z=2.782X1-1.287X2+4.200X3-2.148X4+3.876. The rate of miss-classification was 7.7% in 52 cases when these 4 variables were used. Even if one P-CPR determinant was taken, the incidence of miss-classification was defined as 12.5%. Therefore, if we were to take P-CPR to distinguish IDDM from **NIDDM**, about 77% of the unclassified group could be re-classified into the IDDM group. These results suggest that P-CPR might be better than the other variables for discriminating between IDDM and **NIDDM** in patients whose **diabetes** had been **treated** with insulin. (author abst.)

5/7/150 (Item 2 from file: 94)
DIALOG(R)File 94:JICST-EPlus

01716704 JICST ACCESSION NUMBER: 93A0068224 FILE SEGMENT: JICST-E
Clinical investigation of a case with primary **diabetes** accompanied by chronic pancreatitis. Modification of pancreatic endocrine function due to pancreatic exocrine dysfunction.
WAKASUGI HIDEYUKI (1); OSHIMA AKIRA (1)
(1) National Kyushu Cancer Center Hospital
Iryo(Japanese Journal of National Medical Services), **1992**, VOL.46,NO.11, PAGE.902-906, FIG.1, TBL.2, REF.11
JOURNAL NUMBER: F0707AAZ ISSN NO: 0021-1699 CODEN: IRYOA
UNIVERSAL DECIMAL CLASSIFICATION: 616.39 616.3
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Short Communication
MEDIA TYPE: Printed Publication
ABSTRACT: We studied pathophysiology and diagnosis of pancreatic **diabetes** by investigating exocrine and endocrine pancreatic functions in a male patient with both primary **diabetes** (**NIDDM**) and chronic pancreatitis and those in his sister who had primary **diabetes** alone. The former showed pancreatic calcification, significantly decreased pancreatic exocrine functions and low levels of serum fat-soluble vitamins. Furthermore, byperglycemia and elevated HbA1 values were not as drastic as the latter's. However, in the male patient, the secretion of endogenous insulin (CPR) was greatly decreased and the arginine tolerance test demonstrated a gradual decrease of blood IRG (pancreatic **glucagon**) with time. He first suffered from primary **diabetes** and later pancreatic **diabetes**. His **diabetes** is now thought to have originated from pancreatic **diabetes** and the **treatment** should be according to that of "pancreatic **diabetes**" patients. Measurement of IRG is commonly useful for the diagnosis at this moment. (author abst.)

5/7/151 (Item 3 from file: 94)
DIALOG(R)File 94:JICST-EPlus

01559104 JICST ACCESSION NUMBER: 92A0430918 FILE SEGMENT: JICST-E
Clinical Application of Artificial Pancreas.
ISHIDA YOSHIHIKO (1); KAZUMI TSUTOMU (1); MAEDA TETSUO (1); HOTTA KAZUHIKO (1); YOSHIDA MUNEYOSHI (1); SHII KOZUI (2); BABA SHIGEAKI (2)
(1) Hyogokenritsuseijinbyosenta; (2) Hyogokenseijinbyorinshoken
Hyogo Kenritsu Seijinbyo Senta Kiyo(Bulletin of Hyogo Medical Center for Adults), **1990**, VOL.7, PAGE.1-4, FIG.2, TBL.2, REF.7
JOURNAL NUMBER: Y0270BAQ ISSN NO: 0913-8927
UNIVERSAL DECIMAL CLASSIFICATION: 616/618-76/78 616.39-08
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: Insulin resistance and pancreatic .BETA. cell dysfunction are the predominant features of the patients with **type II** **diabetes** mellitus. There are several methods to estimate the sensitivity of tissue to insulin. Insulin tolerance test is one of the methods. But this is not an accurate method because counterregulatory hormones such as **glucagon**, growth hormone, and cathecolamines have been released due to hypoglycemia which may occur during the test. Therefore, it must be necessary that the level of various hormones which regulate blood glucose are stable during the estimation of insulin effect. Euglycemic glucose clamp technic using Biostator is the only method for that purpose now. So we estimated 25 subjects with

diabetes mellitus and investigated the mechanisms of insulin resistance using Biostator. There was negative correlation between body mass index and insulin resistance which was estimated as glucose utilization. In one patient who had severe insulin resistance, further studies including insulin receptor number, its autophosphoryration and its tyrosin kinase activity were done. It has recently been reported that insulin resistance is associated not only with **diabetes** mellitus but also with atherosclerosis, tumorigenesis and hypertension. Thus, it is very important to characterize the mechanism of insulin resistance in prevention, diagnosis and **treatment** of a variety of diseases. (author abst.)

5/7/152 (Item 4 from file: 94)
DIALOG(R)File 94:JICST-EPlus

01345518 JICST ACCESSION NUMBER: 91A0614775 FILE SEGMENT: JICST-E
A of Study Serial Plasma Islet Amyloid Polypeptide (IAPP) Levels in an Obese **NIDDM** Patient Associated with Diabetic Ketoacidosis.
MITSUKAWA TOMOHIRO (1); TOSHIMORI HIROTAKA (1); NAKAZATO MASAMITSU (1); TAKEMURA JIRO (1); MATSUKURA SHIGERU (1)
(1) Miyazaki Medical College
Tonyobyo(Journal of the Japan Diabetic Society), **1991**, VOL.34,NO.6, PAGE.543-548, FIG.2, TBL.2, REF.16
JOURNAL NUMBER: Z0279BAU ISSN NO: 0021-437X
UNIVERSAL DECIMAL CLASSIFICATION: 616.39
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: We repoirt a study of serial plasma IAPP levels in an obese **NIDDM** patient associated with diabetic ketoacidosis. The patient was an obese 20-year-old male. On September 13, 1989, he was admitted to our hospital because of diabetic ketoacidosis. On admission, urine CPR was 25.7.MU.g/day, and plasma CPR and IAPP responses to **glucagon** injection were low. The patient was **treated** with continuous subcutaneous insulin injection(CSII). Three months later, urine CPR was 64.2.MU.g/day, and after gradually reducing the insulin dose, he was finally **treated** with diet alone under good glycemic control. Plasma IAPP response to **glucagon** became normal along with recovery of C-peptide secretion. This, resulst clearly suggest that plasma IAPP response reflects pancreatic B-cell function in **NIDDM** patients and could be used another index of B-cell function. (author abst.)

5/7/153 (Item 5 from file: 94)
DIALOG(R)File 94:JICST-EPlus

01233634 JICST ACCESSION NUMBER: 91A0270289 FILE SEGMENT: JICST-E
The usefulness of a meal loading test in estimating pancreatic .BETA.-cell secretory function. Comparison with the **glucagon** loading test and with the urinary excretion volume of C-peptide for 24 hours.
HIROTA NORIHIKO (1)
(1) Hirosaki Univ., School of Medicine
Hirosaki Igaku(Hirosaki Medical Journal), **1991**, VOL.42,NO.4, PAGE.436-446, FIG.10, TBL.2, REF.21
JOURNAL NUMBER: F0651AAB ISSN NO: 0439-1721 CODEN: HIRIA
UNIVERSAL DECIMAL CLASSIFICATION: 616-074 616.39
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan

DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: It is important for diabetic patients to estimate .BETA.-cell secretory function in the diagnosis of clinical type of **diabetes** mellitus and in the choice of diabetic **treatments**. To estimate the .BETA.-cell secretory function, the usefulness to clear C-peptide (CPR) response during a meal loading test was studied in patients with non insulin dependent **diabetes** mellitus(**NIDDM**). The increase in CPR of serum (.DELTA.2SCPR) and of urine (.DELTA.2UCPR) during two hours after loading the test meal, and the urinary excretion volume of CPR for 24 hours (24UCPR) were measured on two consecutive days in 48 patients without clinical nephropathy. .DELTA.2UCPR on the first day was significantly and positively correlated with those on the second day ($r=0.70$, $p<0.001$). There was a significant positive correlation between the increase in CPR at 6 minutes after **glucagon** load (.DELTA.6CPR) and .DELTA.2UCPR ($r=0.55$, $p<0.001$). .DELTA.2UCPR in patients with insulin **treatment** was less than 20.MU.g/gvcreatinine. These results indicated that the .BETA.-cell secretory function could be easily estimated by measuring .DELTA.2UCPR in the meal loading test, and that the .DELTA.2UCPR might be useful for diabetic outpatients. (author abst.)

5/7/154 (Item 6 from file: 94)
DIALOG(R)File 94:JICST-EPlus

01124286 JICST ACCESSION NUMBER: 90A0824689 FILE SEGMENT: JICST-E
Effect of nipradilol on carbohydrate metabolism in diabetic patients (**NIDDM**) with hypertension.
FUJII KATSUMI (1); ARISAKA TOMOYUKI (1); TOOJIMA TOSHIO (1); MOCHIZUKI KENTARO (1); HIROSE TOSHIKAZU (1)
(1) Juntendo Univ., School of Medicine
Ther Res, **1990**, VOL.11,NO.8, PAGE.2711-2721, FIG.10, REF.17
JOURNAL NUMBER: Y0681AAP ISSN NO: 0289-8020
UNIVERSAL DECIMAL CLASSIFICATION: 615.225.03 616.12-085:615.22
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: We examined the effect of nipradilol on carbohydrate metabolism, nipradilol (6mg/day) was orally **administered** to 10 non-insulin-dependent-diabetic patients (**NIDDM**) for 2 weeks. Intravenous glucose tolerance test and euglycemic clamp test were investigated in all patients before and after 2 weeks **treatment** with nipradilol. While no significant change was found in the glucose tolerance, insulin responce to glucose and insulin sensitivity, .DELTA.CPR/.DELTA.BS*100 (10, 20 and 30min) were significantly increased during **treatment** ($p<0.05$). We also checked FBS, HbA1c, fructosamine, T-cholesterol, triglyceride, total lipid, NEFA, growth hormone, cortisol and **glucagon**. **Glucagon** was significantly depressed during **treatment**. We concluded that nipradilol may have a beneficial effect on pancreatic .BETA. cell function and have an "anti-diabetogenic effects". (author abst.)

5/7/155 (Item 7 from file: 94)
DIALOG(R)File 94:JICST-EPlus

00946213 JICST ACCESSION NUMBER: 90A0012522 FILE SEGMENT: JICST-E

Usefulness of **glucagon** and arginine test in diabetics.
SOWA RYOICHI (1)
(1) Wakayama Medical College
Wakayama Igaku(Journal of the Wakayama Medical Society), **1989**, VOL.40,NO.3, PAGE.387-398, FIG.11, TBL.3, REF.30
JOURNAL NUMBER: F0546AAI ISSN NO: 0043-0013 CODEN: WKMIA
UNIVERSAL DECIMAL CLASSIFICATION: 616.39
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: To assess the clinical usefulness of **glucagon** test (1mg i.v.) and arginine test (4g i.v.), acute insulin secretion to **glucagon** (.DELTA.G) and arginine (.DELTA.A) were investigated in relation to insulin requirement and disease type classification of **diabetes** mellitus. Each .DELTA. value represented the difference of plasma C-peptide values between basal and 5min after intravenous injection of respective secretagogue. In the patients whose metabolic control were well and stable, all patients with insulin dependent **diabetes** mellitus (IDDM) and 72% of insulin-**treated** non-insulin dependent **diabetes** mellitus (**NIDDM**) had .DELTA.G less than 0.80ng/ml, and when .DELTA.G was over 0.80ng/ml the prevalence of insulin-**treated** patients was remarkablely decreased. In the patients with **NIDDM** who hospitalized for insulin **treatment** because of poor metabolic control, the .DELTA.G at the time of admission could discriminate those who were able to become free from insulin at a later date from those who had to continue insulin **treatment**, but plasma C-peptide response during oral glucose tolerance test and 24 hour urinary C-peptied excretion failed to distinguish the two groups. Moreover, the .DELTA.G colud predict the intensity of insulin therapy. To study the characteristics of pancreatic B cell function in IDDM and **NIDDM**, .DELTA.A was also examined in combination to .DELTA.G. In **NIDDM**, although both .DELTA.G and .DELTA.A were significantly decreased, .DELTA.G/.DELTA.A ratio was not significantly different from that in normals. In the patients with early stage of IDDM, the .DELTA.G was markedly low but .DELTA.A was relatively retained, resulting in significantly low .DELTA.G/.DELTA.A ratio in contrast to that in **NIDDM**. (abridged author abst.)

5/7/156 (Item 8 from file: 94)
DIALOG(R)File 94:JICST-EPlus

00801464 JICST ACCESSION NUMBER: 89A0622740 FILE SEGMENT: JICST-E
Assessment of the residual B-cell function of diabetics. (Part 2). Study on the serum CPR response after meal load.
ENDO MOTOO (1); YAMASHITA AKIKO (1); TANAKA NAHOKO (1); TAKEUCHI HITOSHI (1); AOKI TSUGUAKI (1); MIYATA HAJIME (1); AOYAMA KOHTA (1); OSADA HIDEYUKI (1); WATANABE KOUICHI (1)
(1) Nihon Univ., School of Medicine
Nichidai Igaku Zasshi(Journal of Nihon University Medical Association), **1989**, VOL.48,NO.6, PAGE.513-517, FIG.5, REF.8
JOURNAL NUMBER: F0911AAO ISSN NO: 0029-0424 CODEN: NICHA
UNIVERSAL DECIMAL CLASSIFICATION: 616.39-07
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: To evaluate the residual B-cell function, the serum C-peptide(CPR) response after meal load was assayed in diabetic

patients and correlated with the 24-hour urinary CPR excretion and CPR response after **glucagon** imposition. 1) The meal index (serum CPR at 2 hours after meal-serum CPR before meal)/(plasma glucose at 2 hours after meal-plasma glucose before meal)!*1,000 was 16.4.+-.5.6 in the insulin-**treated NIDDM** group, 43.6.+-.10.0 in the hypoglycemic agents-**treated** group, and 191.0.+-.87.4 in the diet regimen group. The differences among the groups were significant($p<0.001$). 2) There was a significant correlation between the meal index and 24-hour urinary CPR excretion($p<0.01$) and the increment of CPR at 5min after **glucagon** injection($p<0.01$). Investigation of the serum CPR response after meal load is a simple proceudre with no serious invasion of the patient. Our results suggest the possibility of its being used as a therapeutic index for the residual B-cell function in diabetics.(author abst.)

5/7/157 (Item 9 from file: 94)
DIALOG(R)File 94:JICST-EPlus

00792511 JICST ACCESSION NUMBER: 89A0604010 FILE SEGMENT: JICST-E
Studies of plasma pancreatic polypeptide(PP) in diabetics and plasma and pancreatic PP contents in alloxan diabetic dogs.
INOUE YUKIKO (1)
(1) Tokyo Women's Medical College
Tokyo Joshi Ika Daigaku Zasshi(Journal of Tokyo Women's Medical College), **1989**, VOL.59,NO.9, PAGE.1141-1153, FIG.5, TBL.1, REF.53
JOURNAL NUMBER: G0684AAY ISSN NO: 0040-9022 CODEN: TJIZA
UNIVERSAL DECIMAL CLASSIFICATION: 616.39
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication
ABSTRACT: Plasma pancreatic polypeptide(PP) levels in human diabetics, and plasma and pancreatic PP contents in alloxan diabetic dogs were investigated. The results are as follows: 1) After beef soup ingestion, plasma PP levels in untreated non-insulin dependent diabetics (**NIDDM**) increased significantly from 316.+-.195 to 1219.+-.567pg/ml before diabetic **treatment**, and from 339.+-.175 to 1131.+-.168pg/ml after diabetic **treatment**, and were similar to those in controls. 2) No statistical differences in plasma PP levels after beef soup ingestion were found among diabetics **treated** for **NIDDM**, insulin dependent diabetics (IDDM), and controls. 3) Plasma PP levels in basal and postprandial states were not significantly different in poorly-controlled diabetics **treated** by continuous subcutaneous insulin infusion for IDDM, and controls. 4) In alloxan diabetic dogs, the responses of plasma PP and **glucagon** to beef soup ingestion were significantly high compared with those of healthy dogs, although the contents of pancreas PP and **glucagon** in alloxan diabetic dogs and controls were not significantly different in any region of the pancreas. 5) The differences in plasma PP responses in human diabetics and alloxan diabetic dogs may be attributed to the differences between species.(author abst.)

5/7/158 (Item 10 from file: 94)
DIALOG(R)File 94:JICST-EPlus

00196717 JICST ACCESSION NUMBER: 86A0126546 FILE SEGMENT: JICST-E
Qwantitative changes of the pancreatic islets of the non-insulin dependent **diabetes** mellitus (**NIDDM**).

ENOKI NOBORU (1); YOSHIMITSU MITSUO (1); MURATA YOSHIRO (1)
(1) Nara Medical Univ.
Horumon to Rinsho(Clinical Endocrinology), **1985**, VOL.33,NO.11,
PAGE.1071-1075, FIG.1, TBL.4, REF.14
JOURNAL NUMBER: Z0648AAZ ISSN NO: 0045-7167 CODEN: HORIA
UNIVERSAL DECIMAL CLASSIFICATION: 616.39-07
LANGUAGE: Japanese COUNTRY OF PUBLICATION: Japan
DOCUMENT TYPE: Journal
ARTICLE TYPE: Original paper
MEDIA TYPE: Printed Publication

5/7/159 (Item 1 from file: 103)
DIALOG(R)File 103:Energy SciTec

02214665 AIX-19-083621; EDB-88-157405
Author(s): Naidoo, C.
Title: Studies on insulin secretion and insulin resistance in non-insulin-dependent **diabetes** in young Indians
Corporate Source: Natal Univ., Durban (South Africa)
Publisher: Natal Univ.,Durban, South Africa
Publication Date: **1986**
p 151
Academic Degree: Thesis (Ph.D.).
Language: English
Availability: Registrar, University of Natal, King George Avenue, Durban, 4001, South Africa.
Abstract: Patients with Non-insulin-dependent **diabetes** mellitus (**NIDDM**) have defects in insulin secretion and insulin action. In the discrete genetic syndrome of NIDDY (non-insulin-dependent **diabetes** in the young), the situation is less clear and these aspects is the subject of this thesis. This study included Indian pasients with three generation transmission of **NIDDM** via one parent. The insulin and C-peptide responses to oral and intravenous glucose in patients with NIDDY were studied. The insulin and glucose responses to non-glucose secretogogues **glucagon**, tolbutamide and arginine, in NIDDY were also investigated. The following aspects with regard to insulin resistance in NIDDY were examined: glucose and free fatty acid response to intravenous insulin administration, insulin binding to circulating erythrocytes and monocytes, /sup 125/I-insulin binding to the solubilized erythrocyte membrane receptor and /sup 125/I-insulin binding to fibroblasts in culture.

5/7/160 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

09205720 PASCAL No.: 90-0374902
Bedtime insulin for suppression of overnight freefatty acid. blood glucose, and glucose production in **NIDDM**
TASKINEN M R; SANE T; HELVE E; KARONEN S L; NIKKILA E A; YKI-JARVINEN H
Univ. Helsiniki, second & third dep. medicine, Helsinki 00290, Finland
Journal: Diabetes (New York), **1989**, 38 (5) 580-588
ISSN: 0012-1797 CODEN: DIAEAZ Availability: CNRS-8261
No. of Refs.: 49 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: English
Amelioration du controle glycemique par administration d'une insuline dans la soiree (diminution de la production nocturne du glucose)

5/7/161 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

08970816 PASCAL No.: 90-0138952
Long-term effects of dietary fructose on carbohydrate metabolism in non-insulin-dependent **diabetes** mellitus
THORBURN A W; CRAPO P A; GRIVER K; WALLACE P; HENRY R R
Univ. California, dep. medicine, San Diego CA 92161, USA
Journal: Metabolism, clinical and experimental, **1990**, 39 (1) 58-63
ISSN: 0026-0495 Availability: CNRS-6965
No. of Refs.: 26 ref.
Document Type: P (Serial) ; A (Analytic)
Country of Publication: USA
Language: English
The effect of dietary fructose on glycemic control in subjects with **diabetes** mellitus is controversial. Therefore our aim was to conduct a long-term study to examine the effects of dietary fructose on glucose tolerance and insulin sensitivity and to delineate the mechanism for the effects observed. Six subjects with non-insulin-dependent **diabetes** mellitus (**NIDDM**) who were being **treated** by diet alone consumed 13% of their calories as fructose incorporated into mixed meals in place of sucrose for 3 months as inpatients on a metabolic ward

5/7/162 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09660405 PMID: 1297606
Bed time NPH-insulin plus combined sulfonylurea-biguanide oral therapy for **treating** refractory non insulin dependent diabetic patients.
di Cianni G; Benzi L; Ciccarone A M; Cecchetti P; Navalesi R
Diabete & metabolisme (FRANCE) Nov-Dec **1992**, 18 (6) p468-9, ISSN 0338-1684 Journal Code: 7604157
Document type: Letter
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Record Date Created: 19930503
Record Date Completed: 19930503

5/7/163 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09566709 PMID: 1478158
Glucagon -glucose (GG) test for the estimation of the insulin reserve in **diabetes**.
Miki H; Matsuyama T; Fujii S; Komatsu R; Nishioeda Y; Omae T
Department of Medicine, National Cardiovascular Center Hospital, Osaka, Japan.
Diabetes research and clinical practice (NETHERLANDS) Nov **1992**, 18 (2) p99-105, ISSN 0168-8227 Journal Code: 8508335
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The residual B-cell function was examined by means of the plasma

C-peptide response 6 min after a combined injection of **glucagon** and glucose (GG test) or conventional **glucagon** test (G test) in four insulin-dependent diabetic patients (IDDM group), in 18 diabetic patients **treated** with insulin (Insulin group), 31 **treated** with oral hypoglycemic agents (SU group) and 27 **treated** with diet only (Diet group) and in 22 borderline cases. By GG test, 6-min C-peptide values of the IDDM group were 0.27 +/- 0.05 nM (n = 4) and were significantly lower than those of the Insulin group (0.89 +/- 0.09 nM, n = 12), the SU group (1.42 +/- 0.10 nM, n = 13), the Diet group (2.47 +/- 0.22 nM, n = 11) and the borderline cases (3.38 +/- 0.22 nM, n = 11). Patients with a 6-min C-peptide concentration below 0.75 nM by GG test appeared to be insulin-requiring patients. In the G test, plasma C-peptide concentrations at 6 min were 0.35 +/- 0.08 nM in the IDDM group (n = 2), 0.72 +/- 0.20 nM in the Insulin group (n = 7), 1.08 +/- 0.09 nM in the SU group (n = 20), 1.40 +/- 0.19 nM in the Diet group (n = 17) and 2.05 +/- 0.21 nM in the borderline cases (n = 12). Some of the Diet group patients showed extremely low C-peptide responses. When comparing the GG test and G test in individual cases, a greater C-peptide response was seen with the GG test in all cases except for IDDM patients.(ABSTRACT TRUNCATED AT 250 WORDS)

Record Date Created: 19930209
Record Date Completed: 19930209

5/7/164 (Item 3 from file: 155)

09559371 PMID: 1361917

Glucagon , insulin and somatostatin secretion in response to sympathetic neural activation in streptozotocin-induced diabetic rats. A study with the isolated perfused rat pancreas in vitro.

Kurose T; Tsuda K; Ishida H; Tsuji K; Okamoto Y; Tsuura Y; Kato S; Usami M; Imura H; Seino Y

Department of Metabolism and Clinical Nutrition, Kyoto University Faculty of Medicine, Japan.

Diabetologia (GERMANY) Nov **1992**, 35 (11) p1035-41, ISSN 0012-186X Journal Code: 0006777

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Changes in **glucagon**, insulin and somatostatin secretion induced by electrical splanchnic nerve stimulation were examined in rats **treated** with streptozotocin as neonates and as adults. In order to study the direct neural effects we used the isolated perfused rat pancreas with intact left splanchnic nerve in vitro. In normal rats splanchnic nerve stimulation causes significant decreases in insulin (30-40%) and somatostatin (30-50%) secretion at both 16.7 mmol/l and 1 mmol/l glucose concentrations. In the neonatal streptozotocin-diabetic rat splanchnic nerve stimulation at 16.7 mmol/l glucose decreased insulin secretion (14%) further than in the control rats (30%), however, somatostatin secretion did not decrease to the same extent. Similar results were also observed at the low (1 mmol/l) glucose concentration. On the other hand, percent decreases of insulin and somatostatin secretion induced by splanchnic nerve stimulation in the streptozocin-diabetic rats were similar to the values observed in the normal control rats. The **glucagon** secretion in response to splanchnic nerve stimulation at 16.7 mmol/l glucose from pancreatic Alpha cells in both types of induced **diabetes** is exaggerated, and the degree of exaggeration seems to parallel the severity of the hyperglycaemia. However, the splanchnic nerve stimulation-induced **glucagon** secretion at 1 mmol/l glucose was impaired in the streptozotocin-diabetic rats, but not in the neonatal streptozotocin-diabetic rats. These data suggest that the

sensitivity of diabetic Alpha and Delta cells to sympathetic neural activation are blunted, whereas the sensitivity of Beta cells is enhanced in the diabetic animal model.
Record Date Created: 19930201
Record Date Completed: 19930201

5/7/165 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09516136 PMID: 1442097
Increase of blood glucose concentrations in diabetic patients with **glucagon** eyedrops.
Chuang L M; Wu H P; Chiou G C
Department of Internal Medicine, National Taiwan University Hospital, Taipei, China.
Zhongguo yao li xue bao = Acta pharmacologica Sinica (CHINA) May **1992**, 13 (3) p193-7, ISSN 0253-9756 Journal Code: 8100330
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hypoglycemic crisis is a common occurrence in diabetic patients. In order to reverse the hypoglycemia, **glucagon** eyedrops at concentrations of 2.5%, 5.0%, and 7.5% were instilled to the eyes of diabetic patients who were fasted overnight. The **glucagon** eyedrops raised the blood glucose efficiently in a dose-dependent manner and peaked at 30 min after drug instillation. At 2.5%, **glucagon** raised the blood glucose 0.83 mmol.L-1 which exceeded the minimal requirement of 0.56 mmol.L-1 increase in blood glucose level at hypoglycemic crisis. At 5.0% and 7.5%, **glucagon** eyedrops increased the blood glucose level further to 1.76 and 1.91 mmol.L-1, respectively. These results indicate that **glucagon** can be delivered effectively through ocular route to raise the systemic blood glucose for the **treatment** of hypoglycemic crisis.
Record Date Created: 19921209
Record Date Completed: 19921209

5/7/166 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09489789 PMID: 1358326
C-peptide response to **glucagon** in patients with non-insulin-dependent **diabetes** mellitus.
Juang J H; Huang H S; Huang M J
Department of Internal Medicine, Chang Gung Memorial Hospital, Taipei, Taiwan, R.O.C.
Journal of the Formosan Medical Association = Taiwan yi zhi (HONG KONG) May **1992**, 91 (5) p491-6, ISSN 0929-6646 Journal Code: 9214933
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
To understand pancreatic beta cell function in patients with non-insulin-dependent **diabetes**, we analyzed C-peptide response to **glucagon** in 101 nonketotic patients with onset of **diabetes** at over 25 years of age and duration of **diabetes** of more than one year. The fasting serum C-peptide values (FCP), maximal incremental (delta CP) and 6-minute (6'CP) serum C-peptide values after 1 mg of intravenous **glucagon** administration were not related to age at diagnosis (r =

0.12, 0.06 and 0.10, respectively), duration of **diabetes** (r = 0.15, 0.05 and 0.10, respectively), fasting plasma glucose concentrations (r = 0.01, 0.18 and 0.12, respectively) or glycohemoglobin (HbA1c, r = 0.13, 0.22 and 0.16, respectively). In contrast, they showed a clear positive correlation with body mass index (BMI, r = 0.36, 0.52 and 0.41, p < 0.001). In order to evaluate the beta cell function in patients with different responses to **treatment** modalities, a subgroup of 45 patients was divided into three groups: diet successes (DS, n = 14), oral hypoglycemic agent (OHA) successes (OS, n = 19) and OHA failure (OF, n = 12). Among the three groups, patients in the OF group had the longest duration of **diabetes** (9.4 +/- 1.9 years) and the lowest BMI (19.3 +/- 1.0 kg/m2). Serum C-peptide responses to **glucagon** were different in the three study groups. Patients in the DS group had the highest response and patients in the OF group had the lowest response. However, the differences in mean FCP, delta CP and 6'CP among the three groups were not statistically significant, and there was a wide overlap of individual C-peptide values.(ABSTRACT TRUNCATED AT 250 WORDS)
Record Date Created: 19921218
Record Date Completed: 19921218

5/7/167 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09478438 PMID: 1413602
[The dynamics of glucose homeostasis in non-insulin-dependent diabetics under the influence of mineral water intake]
Dinamika glikogomeostaza u bol'nykh insulinnezavisimym sakharnym diabetom pod vliianiem priema mineral'nykh vod.
Krashenitsa G M; Botvineva L A
Voprosy kurortologii, fizioterapii, i lechebnoi fizicheskoi kultury (RUSSIA) May-Jun **1992**, (3) p21-4, ISSN 0042-8787
Journal Code: 2984868R
Document type: Journal Article ; English Abstract
Languages: RUSSIAN
Main Citation Owner: NLM
Record type: Completed
The paper presents time course changes registered in glycohomeostasis of patients suffering from non-insulin-dependent **diabetes** mellitus (**NIDDM**) as a result of a single or course intake of acidulous chloride hydrocarbonate sodium mineral waters. The **treatment** promoted immediate or delayed improvement in glycemia and insulinemia control, correction of imbalance of hormonal glycohomeostasis regulators (insulin, **glucagon**), enhancement of gastrinemia. The insulinotrophic effect varied with mineralization of the water, concentrations of bicarbonate and sodium ions. Water regimens were specified for **NIDDM** patients.
Record Date Created: 19921026
Record Date Completed: 19921026

5/7/168 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09429547 PMID: 1520901
A simple clinical approach to discriminate between "true" and "pseudo" secondary failure to oral hypoglycaemic agents.
Scionti L; Misericordia P; Santucci A; Santeusanio F; Brunetti P
Istituto di Medicina Interna e Scienze Endocrine e Metaboliche, University of Perugia, Italy.
Acta diabetologica (GERMANY) **1992**, 29 (1) p20-4, ISSN

0940-5429 Journal Code: 9200299
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

To discriminate between true secondary failure (TF) and pseudo-secondary failure (PF) to oral hypoglycaemic agents, we studied 34 non-obese non-insulin-dependent diabetic patients who were being **treated** with these drugs. Nine were in good control (GC) with oral **treatment**, while 25 showed apparent SF. During a controlled hospital diet, fasting blood glucose remained persistently high in 15 of these patients (TF), while in the other 10 patients it clearly improved (PF). Fasting plasma glucose (FPG) and HbA1c were higher and body mass index (BMI) was lower in TF patients than in PF patients (P less than 0.01). C-peptide concentrations differed significantly among the three groups both in the fasting state (TF 0.25 +/- 0.02 nmol/l, PF 0.70 +/- 0.03 nmol/l, GC 0.74 +/- 0.03 nmol/l; P less than 0.0001) and 6 min after **glucagon** injection (TF 0.50 +/- 0.04 nmol/l, PF 1.02 +/- 0.06 nmol/l, GC 1.14 +/- 0.07 nmol/l; P less than 0.0001). C-peptide and plasma insulin curves obtained after a standard mixed meal also showed significant differences (P less than 0.001). In particular, there was a statistically significant difference between GC and PF versus TF (P less than 0.05), while there was no statistical difference between PF and GC. We conclude that some patients with apparent SF can improve their metabolic control if they strictly adhere to a correct diet (PF); a single measurement of basal C-peptide concentration or examination of the C-peptide and insulin responses to a meal are useful indicators for distinguishing patients with PF from those with TF to oral hypoglycaemic agents.(ABSTRACT TRUNCATED AT 250 WORDS)

Record Date Created: 19921015
Record Date Completed: 19921015

5/7/169 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09399583 PMID: 1499870

Banting Lecture: glucose turnover. A key to understanding the pathogenesis of **diabetes** (indirect effects of insulin).

Vranic M
Department of Physiology, Faculty of Medicine, University of Toronto, Canada.

Diabetes (UNITED STATES) Sep **1992**, 41 (9) p1188-206, ISSN 0012-1797 Journal Code: 0372763
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

This article is divided into two parts. A retrospective overview summarizes some of the work that provided the framework and tools of the more recent studies. The five novel areas of research are related to the indirect effects of insulin. Regulation of plasma glucose is of central importance in health and **diabetes** . Understanding this precise regulation requires sensitive isotope dilution methods that can measure the rates at which glucose is produced by the liver and used by the tissues on a minute-to-minute basis. Validation studies indicated that the non-steady-state tracer method yields reasonable results when the specific activity of plasma glucose does not change abruptly. During hyperinsulinemic glucose clamps, the decrease in specific activity of glucose can be prevented by the MSTI. During exercise, the decrease of specific activity can be only in part ameliorated by step-tracer infusion. Depancreatized dogs are used extensively as a model of selective insulin

deficiency, because dog stomach secretes physiological amounts of **glucagon** . This strategy can avoid injections of somatostatin, which can have other affects in addition to the suppression of insulin and **glucagon**. In human **diabetes** , in addition to an increase of glucose production, there is also an increase in glucose cycling in the liver. In animal models of **diabetes**, mild **NIDDM**, and in glucose intolerance, the percentage of increments of glucose cycling are much larger than those of glucose production. We hypothesize, therefore, that measurements of glucose cycling can be used as an early marker of glucose intolerance. Application of different tracer strategies and use of the depancreatized dog as a model of **diabetes** , we investigated the importance of the indirect effects of insulin in the pathogenesis of **diabetes**. 1) Because, in the **treatment** of IDDM, insulin is **administered** by the peripheral routes we compared the relative importance of hepatic and peripheral effects of insulin in regulating the rate of glucose production. Experiments were performed in depancreatized dogs that were initially maintained at moderate hyperglycemia (10 mM) with subbasal portal insulin infusion. During the experimental period, insulin was infused either peripherally or portally at 0.9 mU.kg-1.min-1. In addition, peripheral infusions were also given at 0.45 mU.kg-1.min-1. We concluded that when suprabasal insulin levels are provided to moderately hyperglycemic depancreatized dogs, the suppression of glucose production is more dependent on peripheral than portal insulin concentrations. This indirect effect of insulin may be mediated by limitation of the flow of precursors and energy substrates for gluconeogenesis and/or by suppressive effect of insulin on **glucagon** secretion.(ABSTRACT TRUNCATED AT 400 WORDS) (187 Refs.)

Record Date Created: 19920917
Record Date Completed: 19920917

5/7/170 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09399001 PMID: 1499473

Comparison of combined therapies in **treatment** of secondary failure to glyburide.

Trischitta V; Italia S; Mazzarino S; Buscema M; Rabuazzo A M; Sangiorgio L; Squatrito S; Vigneri R

Cattedra di Endocrinologia, Universita di Catania, Ospedale Garibaldi, Italy.

Diabetes care (UNITED STATES) Apr **1992**, 15 (4) p539-42, ISSN 0149-5992 Journal Code: 7805975

Document type: Clinical Trial; Journal Article; Randomized Controlled Trial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

OBJECTIVE--To compare the effectiveness of alternative combined **treatments** in patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) with secondary failure to sulfonylureas. RESEARCH DESIGN AND METHODS--A crossover study was carried out by randomly assigning 16 **NIDDM** patients to a combined **treatment** with the addition of either a single low-dose bedtime injection of 0.2 U/kg body wt NPH insulin or an oral three times a day administration of 1.5 g/day metformin to the previously ineffective glyburide **treatment**. RESULTS--Both combined therapies significantly (P less than 0.01) reduced fasting plasma glucose (FPG), postprandial plasma glucose (PPPG) and percentage of HbA1. The addition of metformin was more effective than the addition of insulin (P less than 0.01) in improving PPPG in the 8 patients with higher post-**glucagon** C-peptide levels. In contrast, the efficacy of neither

combined therapy was related to patient age, age of **diabetes** onset, duration of the disease, percentage of ideal body weight, and FPG. The addition of insulin but not metformin caused a significant (P less than 0.01) increase of mean body weight. Neither combined **treatment** caused changes in serum cholesterol and triglyceride levels. No symptomatic hypoglycemic episode was reported in any of the 16 patients. CONCLUSIONS--The addition of bedtime NPH insulin or metformin was effective in improving the glycemic control in most **NIDDM** patients with secondary failure to glyburide. The combination of metformin and sulfonylurea was more effective in reducing PPPG and did not induce any increase of body weight.
Record Date Created: 19920917
Record Date Completed: 19920917

5/7/171 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09397617 PMID: 1498529
Clinical and experimental study of semen Persical decoction for purgation with addition in **type II diabetes** mellitus]
Xiong M Q
Guangzhou College of TCM.
Zhongguo zhong xi yi jie he za zhi Zhongguo Zhongxiyi jiehe zazhi = Chinese journal of integrated traditional and Western medicine / Zhongguo Zhong xi yi jie he xue hui, Zhongguo Zhong yi yan jiu (CHINA) Feb **1992**, 12 (2) p74-6, 67, ISSN 1003-5370 Journal Code: 9211576
Document type: Journal Article ; English Abstract
Languages: CHINESE
Main Citation Owner: NLM
Record type: Completed
This paper reported the results of clinical observation on a **treatment** with Semen Persical decoction for purgation with addition (SPDPA) in **type II diabetes** mellitus. The effective rate of SPDPA on 106 cases of noninsulin dependent **diabetes** mellitus (**NIDDM**) was 79%. The efficiency of SPDPA was equivalent to glyburide. From the experimental study, it can be concluded that SPDPA could reduce blood sugar and relieve symptom in diabetic patients and rats. Its mechanism may be due to improving secretion of insulin, inhibiting production of **glucagon**, repairing insular endocrine cell, increasing endocrine pellet of insular B cell and improving composition of hepatic glycogen. In traditional Chinese medicine theory, the mechanism of therapeutic action of SPDPA in **diabetes** mellitus is based on synergistic regulation of benefiting Qi and nourishing Yin, activating blood circulation to dissipate blood stasis and loosening the bowel to relieve constipation.
Record Date Created: 19920916
Record Date Completed: 19920916

5/7/172 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09394751 PMID: 1496338
Various molecular mechanisms involved in the pathogenesis of **type II diabetes** and their potential therapeutic importance]
Quelques mecanismes moleculaires impliques dans la pathogenese du diabete de **type II** et leur importance therapeutique potentielle.
Waeber G; Nicod P
Departement de medecine interne B, Centre hospitalier universitaire

vaudois, Lausanne.
Schweizerische medizinische Wochenschrift (SWITZERLAND) Jul 25 **1992**, 122 (30) p1109-16, ISSN 0036-7672 Journal Code: 0404401
Document type: Journal Article; Review; Review, Tutorial ; English Abstract
Languages: FRENCH
Main Citation Owner: NLM
Record type: Completed
The pancreatic beta cell presents functional abnormalities in the early stages of development of non-insulin dependent **diabetes** mellitus (**NIDDM**). The disappearance of the first phase of insulin secretion induced by a glucose load is a early marker of **NIDDM** . This abnormality could be secondary to the low expression of the pancreatic glucose transporter GLUT2. Together with the glucokinase enzyme, GLUT2 is responsible for proper beta cell sensing of the extracellular glucose levels. In **NIDDM** , the GLUT2 mRNA levels are low, a fact which suggests a transcriptional defect of the GLUT2 gene. The first phase of glucose-induced insulin secretion by the beta pancreatic cell can be partly restored by the administration of a peptide discovered by a molecular approach, the **glucagon**-like peptide 1 (GLP-1). The gene encoding for the **glucagon** is expressed in a cell-specific manner in the A cells of the pancreatic islet and the L cells of the intestinal tract. The maturation process of the propeptide encoded by the **glucagon** gene is different in the two cells: the **glucagon** is the main hormone produced by the A cells whereas the **glucagon**-like peptide 1 (GLP-1) is the major peptide synthesized by the L cells of the intestine. GLP-1 is an incretin hormone and is at present the most potent insulinotropic peptide. The first results of the administration of GLP-1 to normal volunteers and diabetic patients are promising and may be a new therapeutic approach to **treating** diabetic patients. (40 Refs.)
Record Date Created: 19920908
Record Date Completed: 19920908

5/7/173 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09292472 PMID: 1580598
Pancreas transplantation as therapy for **diabetes** mellitus.
Robertson R P; Sutherland D E
Diabetes Center, University of Minnesota, Minneapolis 55455.
Annual review of medicine (UNITED STATES) **1992**, 43 p395-415, ISSN 0066-4219 Journal Code: 2985151R
Contract/Grant No.: M01 RR 00400; RR; NCRR; R01 DK 39994; DK; NIDDK
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Pancreas transplantation, when successful, is the only reproducibly effective method to normalize glycemia without the use of exogenous insulin **treatment** in patients with **diabetes** mellitus. Worldwide success rates for combined pancreas and kidney transplantation are approximately 70%, and patient survival rates are approximately 90% one year postoperatively, although certain institutions have higher rates. Benefits of this procedure include normalization of fasting plasma glucose, hemoglobin A1C, glucose-induced insulin secretion, and intravenous glucose tolerance. Improvements are observed in glucose recovery following insulin-induced insulin hypoglycemia, **glucagon** secretion during hypoglycemia, kidney structure, and both motor and sensory nerve function. However, no benefits are accrued in pancreatic polypeptide secretion, kidney function, and the retinal pathology of **diabetes** mellitus.

Further progress in these therapeutic results must await improvements in drugs for induction of immunosuppression, methods to induce immune tolerance, or provision of the operative procedure to patients less compromised preoperatively with secondary complications of **diabetes**.
(44 Refs.)
Record Date Created: 19920611
Record Date Completed: 19920611

5/7/174 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09215595 PMID: 1542270
Relationship between blood pressure and **in vivo** action of insulin in **type II** (non-insulin-dependent) diabetic subjects.
Birkeland K I; Chatzipanagiotou F; Hanssen K F; Vaaler S
Hormone Laboratory, Aker University Hospital, Oslo, Norway.
Metabolism- clinical and experimental (UNITED STATES) Mar **1992**, 41 (3) p301-5, ISSN 0026-0495 Journal Code: 0375267
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In nondiabetic hypertensive subjects, a relationship has been found between insulin resistance and level of blood pressure. Since **type II** (non-insulin-dependent) diabetic subjects are often both insulin-resistant and hypertensive, we studied the relationship between insulin resistance and blood pressure level in a group of patients with **type II diabetes**. Fourteen women and 19 men with **diabetes** for 2 to 14 (mean, 7.4) years, **treated** with diet alone (five subjects) or combined with hypoglycemic agents, were studied. Their average hemoglobin A1c (HbA1c) levels during the study period were 6.6% to 11.7% (mean, 8.6%), and their body mass indexes (BMI) were 20.8 to 33.1 (mean, 26.3) kg/m2. Insulin sensitivity was measured using the hyperinsulinemic, euglycemic glucose clamp technique, and an insulin-sensitivity index was calculated as the ratio of the glucose disposal rate (GDR) to the insulin concentration during clamp (GDR/I). The average of three to eight measurements of diastolic blood pressure (DBP) during the study period (9 to 24 months) in each subject was 79 to 111 (mean, 95.1) mm Hg, and DBP also showed significant correlations to BMI (r = .54) and fasting C-peptide level (r = .38). In a multiple regression model, GDR/I, antihypertensive **treatment**, and known duration of **diabetes** were significant and independent predictors of variations in blood pressure, and GDR/I could account for 35% of the observed variations in DBP. We conclude that, in accordance with what has been found in nondiabetic hypertensives, DBP correlates significantly to insulin resistance in **type II** diabetic subjects.
Record Date Created: 19920403
Record Date Completed: 19920403

5/7/175 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09212268 PMID: 1794270
Evaluation of the efficacy and safety of Diamicron in non-insulin-dependent diabetic patients.
Kilo C; Dudley J; Kalb B
Kilo Diabetes and Vascular Disease Research Foundation, St. Louis, Missouri.

Diabetes research and clinical practice (NETHERLANDS) **1991,** 14 Suppl 2 pS79-82, ISSN 0168-8227 Journal Code: 8508335
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The efficacy and safety of gliclazide (Diamicron) were studied in 29 **NIDDM** patients (19 men and 10 women aged 25-68 years) who failed to improve with diet or with diet plus a sulfonylurea. All patients were overweight and had fasting blood glucose levels consistently above 150 mg/dl (8.24 mmol/l). After withdrawal of oral hypoglycemics where applicable, they received 40 mg Diamicron three times daily with meals. The dose was increased by 40-80 mg/day until optimum control was obtained or up to a maximum of 320 mg/day. **Treatment** lasted for 12 months. At the end of this period the mean fasting blood glucose level had fallen by 35% from 238 to 154 mg/dl and the mean 2-h postprandial blood glucose level had fallen by 28% from 237.7 to 195 mg/dl. The mean glycosylated hemoglobin level also fell by 30% from 10.10 to 7.02%, i.e. within the normal range. In addition, there was a 19% fall in triglyceride and a 10% fall in cholesterol levels, with no change in body weight. No changes were observed for serum insulin, C-peptide and **glucagon** levels, thyroid function tests, blood counts, liver and kidney function tests, uric acid, electrolytes, blood pressure or heart rate. No clinical or ECG abnormalities were observed in patients with or without cardiovascular disease. There were two presumptive hypoglycemic reactions, but these did not require **treatment**. Adverse effects were reported by 22 patients, including dizziness and light-headedness, diarrhea, nausea, palpitations and pruritus, but none required modification of Diamicron therapy. The results therefore show that Diamicron is safe, effective and well tolerated in suitably selected **NIDDM** patients.

Record Date Created: 19920406
Record Date Completed: 19920406

5/7/176 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09142123 PMID: 1761065

Influence of short term verapamil **treatment** on glucose metabolism in patients with non-insulin dependent **diabetes** mellitus.

Busch Sorensen M; Sjostrand H; Sengelov H; Tiefenthal Thrane M; Juul Holst J; Lyngsoe J
Medical Department C, Bispebjerg Hospital, Copenhagen Denmark.

European journal of clinical pharmacology (GERMANY) **1991,** 41 (5) p401-4, ISSN 0031-6970 Journal Code: 1256165
Document type: Clinical Trial; Controlled Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The effect of a sustained-release verapamil preparation on glucose metabolism was investigated in 10 patients with non-insulin dependent **diabetes** mellitus. In a single blind cross-over study verapamil 240 mg b.d. for 1 week lowered fasting plasma glucose from a mean value of 11.6 mmol/l to 10.3 mmol.l-1, and the fasting glucose appearance rate was decreased from 1.5 to 1.2 mmol.min-1. The decrease in fasting plasma glucose and glucose appearance rate was not related to the steady state plasma concentration of verapamil, nor-verapamil and the metabolites D.617 and D.620. After oral glucose administration a tendency to lower plasma glucose values was found after verapamil administration. Plasma insulin, C-peptide, total and C-terminal **glucagon** were not significantly different in the placebo and the verapamil studies, neither in the fasting

state nor after glucose. It is concluded that brief verapamil **treatment** decreases fasting plasma glucose and glucose turn-over in non-insulin dependent diabetics, possibly by inhibition of gluconeogenesis.
Record Date Created: 19920212
Record Date Completed: 19920212

5/7/177 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09128312 PMID: 1309325
Insulinotropic hormone **glucagon**-like peptide-I(7-37) stimulation of proinsulin gene expression and proinsulin biosynthesis in insulinoma beta TC-1 cells.
Fehmann H C; Habener J F
Laboratory of Molecular Endocrinology, Massachusetts General Hospital, Howard Hughes Medical Institute, Harvard Medical School, Boston 02114.
Endocrinology (UNITED STATES) Jan **1992**, 130 (1) p159-66, ISSN 0013-7227 Journal Code: 0375040
Contract/Grant No.: DK30834; DK; NIDDK
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Glucagon -like peptide-I(7-37) [GLP-I(7-37)] is an intestinal peptide hormone that is released in response to oral nutrients and that potently augments glucose-mediated insulin secretion. GLP-I(7-37) has potent insulin-releasing activities **in vivo** in response to oral nutrients, in situ in the isolated perfused pancreas, and in vitro in cultured pancreatic B-cells. As such GLP-I(7-37) is a potent hormonal mediator in the enteroinsular axis involved in the regulation of glucose homeostasis. We now show that in addition to stimulating the release of insulin, GLP-I(7-37) stimulates proinsulin gene expression at the levels of gene transcription and cellular levels of proinsulin messenger RNA as well as the translational biosynthesis of proinsulin. These findings of the positive anabolic actions of GLP-I(7-37) on the synthesis of insulin in B-cells support the notion that GLP-I(7-37) may be of therapeutic use in stimulating the production of insulin in patients with noninsulin-dependent **diabetes** mellitus and that overproduction of insulin with subsequent hypoglycemia will not occur in response to the administration of GLP-I(7-37). Furthermore, these positive actions of GLP-I(7-37) on insulin production obviate the possibility of B-cell exhaustion in response to such a potent secretagogue.
Record Date Created: 19920127
Record Date Completed: 19920127

5/7/178 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08995818 PMID: 1872310
Mechanisms for hyperglycemia in **type II diabetes** mellitus: therapeutic implications for sulfonylurea **treatment**--an update.
Porte D; Kahn S E
Department of Medicine, University of Washington School of Medicine, Seattle.
American journal of medicine (UNITED STATES) Jun 24 **1991**, 90 (6A) p8S-14S, ISSN 0002-9343 Journal Code: 0267200
Contract/Grant No.: DK 12829; DK; NIDDK; DK 17047; DK; NIDDK

Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Non-insulin-dependent **diabetes** mellitus (**NIDDM**) is characterized by fasting hyperglycemia associated with defects in the pancreatic islet, the liver, and the peripheral tissues, which together comprise a feedback loop responsible for maintenance of glucose homeostasis. This review focuses on the key role of the endocrine pancreas alpha and beta cells to coordinate glucose output from the liver with glucose utilization. The basal rate of hepatic glucose utilization. The basal rate of hepatic glucose production is elevated in subjects with **NIDDM** , and this is positively correlated with the degree of fasting hyperglycemia. This increased rate of glucose release by the liver results from impaired hepatic sensitivity to insulin, reduced insulin secretion, and increased **glucagon** secretion. Though basal immunoreactive insulin levels in patients with **NIDDM** may appear normal when compared with healthy individuals, islet function testing at matched glucose levels reveals impairments of basal, steady-state, and stimulated insulin secretion due to a reduction in beta-cell secretory capacity and a reduced ability of glucose to suppress **glucagon** . The degree of impaired beta-cell responsiveness to glucose is closely related to the degree of fasting hyperglycemia but in a curvilinear fashion. The efficiency of glucose uptake by the peripheral tissues is also impaired due to a combination of decreased insulin secretion and defective cellular insulin action. This impairment becomes more important to the hyperglycemia as the islet alpha- and beta-cell function declines. Therapeutic interventions, to be effective, must reduce hepatic glucose production either by improving islet dysfunction and raising plasma insulin levels, or improving the effectiveness of insulin on the liver. Both result in a decline in the fasting glucose levels regardless of the cause of hyperglycemia. We conclude that **NIDDM** is characterized by a steady-state re-regulation of plasma glucose concentration at an elevated level in which islet dysfunction plays a necessary role. **Treatment** should be based on this physiologic understanding. (26 Refs.)

Record Date Created: 19910913
Record Date Completed: 19910913

5/7/179 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08987621 PMID: 1867120

Beneficial effects of added glicazide in patients with **type II diabetes** mellitus **treated** with insulin]

Efeitos beneficos da adicao de gliclazida em doentes diabeticos do tipo II sob insulina.

Ruas M M; Carvalheiro M; Geraldes E; Carrilho F; Bastos M; Fagulha A; Paiva I; Rodrigues F; Gomes L

Servico de Endocrinologia e Doencas Metabolicas, Hospitais da Universidade de Coimbra.

Acta medica portuguesa (PORTUGAL) Mar-Apr **1991**, 4 (2) p76-8, ISSN 0870-399X Journal Code: 7906803

Document type: Journal Article ; English Abstract
Languages: PORTUGUESE
Main Citation Owner: NLM
Record type: Completed

The aim of the study was to assess, in patients with non insulin dependent **diabetes** mellitus (**NIDDM**), either with previous failure to sulphonylureas or insulin **treated** since the disease started, if the combination of gliclazide to insulin therapy might induce a

reduction of daily insulin requirement. 30 caucasian **type II** patients used to self-monitoring (11 female, 19 male, mean age 55.78 +/- 8.07) with residual pancreatic function (**glucagon** induced C-peptide release = 1.01 +/- 0.70 microgram/ml) entered the study. 8 were excluded for non compliance or for high antiinsulin antibodies levels and 4 are still under study. Each patients was given, for 3 months, 240 mg of gliclazide in addition to usual daily dose of insulin. Data presented as mean +/- s.e.m. were analysed with analysis of variance (p less than 0.05). Mean initial values of main parameters were as follows: glycaemia 192.7 +/- 33.1 mg/100 ml, insulinaemia 9.5 +/- 4.5 microUI/ml, daily insulin requirements 33.11 +/- 10.47 U/d, HbA1 C 7.5 +/- 1.7%. Total cholesterol 240.1 +/- 52.2 mg/10 ml, triglycerides 120.6 +/- 60.3 mg/100 ml. After 3 months **treatment** significant reduction in mean daily insulin requirements (20.78 +/- 16.15 U/d) was observed. In 13 patients (72.2%) while keeping good metabolic control (HbA1 C 7.46 +/- 1.63), insulin therapy was reduced (9 patients) or even stopped (4 patients). In the other 5, insulin was maintained or slightly increased. The increase in **glucagon** induced C-peptide release (1.41 +/- 0.99 micrograms/ml) did not reach significance, while glycaemia and insulinaemia were not changed (196.0 +/- 34.1 mg/100 ml, 11.02 +/- 5.05 microUI/ml).(ABSTRACT TRUNCATED AT 250 WORDS)

Record Date Created: 19910909
Record Date Completed: 19910909

5/7/180 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08968668 PMID: 1649673

Insulin **treatment** improved glucose-induced insulin release in elderly non-insulin-dependent **diabetes** mellitus, secondary failure to oral hypoglycemic agents.

Jap T S; Kwok C F; Won J G; Ho L T
Division of Endocrinology and Metabolism, Veterans General Hospital-Taipei, R.O.C.

Zhonghua yi xue za zhi = Chinese medical journal; Free China ed (TAIWAN)
May **1991**, 47 (5) p320-4, ISSN 0578-1337 Journal Code: 0005327
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

In order to observe whether the improvement of diabetic control would promote insulin release of elder non-insulin-dependent diabetics, we performed oral glucose tolerance test and **glucagon** infusion in eight patients before and after fasting plasma glucose normalized with insulin therapy for three weeks. The levels of plasma glucose and C-peptide both on fasting and following intravenous **glucagon** infusion and oral glucose loading were measured. Their ages ranged from 60 to 72 years old. The initial fasting plasma glucose levels were 261 +/- 18 mg/dl (Mean +/- SEM). After insulin therapy for three weeks, the fasting plasma glucose levels dropped to 130 +/- 8 mg/dl (Mean +/- SEM, P less than 0.001). The fasting C-peptide/glucose ratio showed no difference before and after therapy. On the other hand, the C-peptidogenic index was markedly improved following insulin therapy, as compared with the value before therapy (P less than 0.05). These results suggested that greater C-peptide response was found in non-insulin dependent elderly diabetics following oral glucose after plasma glucose normalized with insulin therapy.

Record Date Created: 19910827
Record Date Completed: 19910827

5/7/181 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08875635 PMID: 1850647
Clinical significance of measuring serum c-peptide before and after **glucagon** injection]
Kan Y; Chi Z
Zhonghua yi xue za zhi (CHINA) Jan **1991**, 71 (1) p16-7, 4, ISSN 0376-2491 Journal Code: 7511141
Document type: Journal Article ; English Abstract
Languages: CHINESE
Main Citation Owner: NLM
Record type: Completed
To evaluate pancreatic beta-cell secretory activity, c-peptide concentrations before and 6 minutes after an i.v. injection of **glucagon** were measured in 12 normal subjects (group N), 23 diabetics **treated** with diet control and oral antidiabetics (group DI) and 71 patients **treated** with insulin (group DII). The results showed that the fasting c-peptide concentration in group N and group DI were comparable, but significantly higher than that in group DII. An overlap was found between fasting c-peptide from 6 diabetics in group DI and that from group DII. There were significant differences among the c-peptide concentrations 6 minutes after **glucagon** injection in the three groups and there was no overlap between c-peptide in group DI and that in group DII 6 minutes after injection. The above-mentioned data suggest that c-peptide concentration 6 minutes after **glucagon** injection may reflect beta-cell secretory activity better than fasting c-peptide.
Record Date Created: 19910605
Record Date Completed: 19910605

5/7/182 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08808348 PMID: 1981229
Effect of dietary therapy on pancreatic beta cell function in noninsulin-dependent **diabetes** mellitus.
Juang J H; Wang P W; Huang M J
Department of Internal Medicine, Chang Gung Memorial Hospital, Kaohsiung, Taiwan, R.O.C.
Journal of the Formosan Medical Association = Taiwan yi zhi (TAIWAN) Aug **1990**, 89 (8) p672-6, ISSN 0929-6646 Journal Code: 9214933
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Twenty-four noninsulin-dependent diabetics, who were newly diagnosed or had discontinued therapy for at least 10 months, were studied for the effect of dietary therapy on pancreatic beta cell function. The mean fasting plasma glucose (176 +/- 14 vs 212 +/- 16 mg/dl, p less than 0.01) and glycosylated hemoglobin (HbA1c, 8.6 +/- 0.5 vs 9.4 +/- 0.6%, p less than 0.001) decreased significantly after 1 month of dietary control, although there was no significant change in mean body weight (57.4 +/- 2.0 vs 57.7 +/- 2.0 kg, p greater than 0.5). The mean incremental serum C-peptide (delta CP) response to oral glucose stimulation (OGTT) increased (4.6 +/- 0.6 vs 3.5 +/- 0.7 ng/ml, p less than 0.01), but that to intravenous **glucagon** (GT) did not (2.5 +/- 0.2 vs 2.7 +/- 0.2 ng/ml, p greater than 0.1). In 12 patients whose glycemic control improved after dietary **treatment**, there was a good correlation between the decrement in fasting plasma glucose and the increment in delta CP response to OGTT (r

= 0.66, p less than 0.05). In conclusion: after 1 month of dietary therapy in noninsulin-dependent diabetics, (1) the serum C-peptide response to OGTT, but not to GT, improved; (2) the beta cell secretion increased only in those patients with improved glycemic control; (3) there was a good correlation between glycemic control and beta cell function.
Record Date Created: 19910401
Record Date Completed: 19910401

5/7/183 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08668766 PMID: 2210074
Actions of novel antidiabetic agent englitazone in hyperglycemic hyperinsulinemic ob/ob mice.
Stevenson R W; Hutson N J; Krupp M N; Volkmann R A; Holland G F; Eggler J F; Clark D A; McPherson R K; Hall K L; Danbury B H; et al
Department of Metabolic Diseases, Pfizer Inc., Groton, Connecticut 06340.
Diabetes (UNITED STATES) Oct **1990**, 39 (10) p1218-27, ISSN 0012-1797 Journal Code: 0372763
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The effects of CP 68722 (racemic englitazone) were examined in ob/ob mice, in adipocytes and soleus muscles from ob/ob mice, and in 3T3-L1 adipocytes. Administration of englitazone at 5-50 mg.kg-1.day-1 lowered plasma glucose and insulin dose dependently without producing frank hypoglycemia in either the diabetic or nondiabetic lean animals. The glucose-lowering effect in ob/ob mice preceded the reduction in hyperinsulinemia. On cessation of drug, plasma insulin returned to untreated levels within 48 h, whereas plasma glucose rose slowly over 5 days. Englitazone (50 mg/kg) for 11 days lowered plasma glucose (22.2 +/- 1.4 to 14.0 +/- 1.9 mM), insulin (7.57 +/- 0.67 to 1.64 +/- 0.60 nM), nonesterified fatty acids (1813 +/- 86 to 914 +/- 88 microM), glycerol (9.20 +/- 0.98 to 4.94 +/- 0.03 mM), triglycerides (1.99 +/- 0.25 to 1.03 +/- 0.11 g/L), and cholesterol (6.27 +/- 0.96 to 3.87 +/- 0.57 mM), but no effects were observed 3 h after a single dose. Basal and insulin-stimulated lipogenesis were enhanced in adipocytes from ob/ob mice **treated** with 50 mg/kg englitazone for 11 days compared with lipogenesis in cells from vehicle-**treated** controls. **Treatment** of ob/ob mice with 50 mg/kg englitazone reversed the defects in insulin-stimulated glycolysis (from [3-3H]glucose) and glycogenesis and basal glucose oxidation (from [1-14C]glucose) in isolated soleus muscles. Englitazone (30 microM) stimulated 2-deoxy-D-glucose transport in 3T3-L1 adipocytes from 0.37 +/- 0.03 to 0.65 +/- 0.06 and 1.53 nmol.min-1.mg-1 protein at 24 and 48 h, respectively. Thus, englitazone has 1) insulinomimetic and insulin-enhancing actions in vitro and 2) glucose-, insulin-, triglyceride-, and cholesterol-lowering properties in an animal model of non-insulin-dependent **diabetes** mellitus (**NIDDM**) in which sulfonylureas have little or no effect. Thus, this new agent may have beneficial effects including a reduced risk of hypoglycemia in patients with **NIDDM**.
Record Date Created: 19901121
Record Date Completed: 19901121

5/7/184 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08635987 PMID: 2167806
Physiological levels of plasma non-esterified fatty acids impair forearm glucose uptake in normal man.
Walker M; Fulcher G R; Catalano C; Petranyi G; Orskov H; Alberti K G
Department of Medicine, University of Newcastle upon Tyne, U.K.
Clinical science (London, England - 1979) (ENGLAND) Aug **1990**, 79 (2) p167-74, ISSN 0143-5221 Journal Code: 7905731
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
1. The purpose of the present study was to maintain physiological plasma non-esterified fatty acid levels and to (i) examine their effect on skeletal muscle insulin-stimulated glucose uptake and metabolite exchange using the forearm technique, and (ii) evaluate their effect on whole-body glucose uptake and fuel oxidation. 2. Intralipid (10%) and heparin (Lipid) or saline (Control) was **administered** to eight healthy male subjects on separate occasions for 210 min. Insulin, **glucagon** and somatostatin were **administered** from 60 to 210 min in each study and euglycaemia was maintained. 3. Plasma non-esterified fatty acid levels plateaued at 420 +/- 50 mumol/l with the Lipid infusion but were completely suppressed during the Control clamp. Forearm non-esterified fatty acid uptake increased with the Lipid infusion (+50 +/- 10 nmol min-1 100 ml-1 of forearm) and was accompanied by a significant decrease in forearm glucose uptake (+3.23 +/- 0.25 versus +3.65 +/- 0.35 mumol min-1 100 ml-1 of forearm, Lipid and Control, respectively; P less than 0.05) and alanine release (-84 +/- 12 versus -113 +/- 15 nmol min-1 100 ml-1 of forearm, Lipid and Control, respectively; P less than 0.05).(ABSTRACT TRUNCATED AT 250 WORDS)
Record Date Created: 19901003
Record Date Completed: 19901003

5/7/185 (Item 24 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08611578 PMID: 2199090
Effect of ke-tang-Ling administration on the function of pancreatic islets cells in non-insulin-dependent **diabetes** mellitus]
Wang Z; Yin Z
Department of Cardio-Endocrinology, Tianjin No 2 Hospital.
Zhong xi yi jie he za zhi = Chinese journal of modern developments in traditional medicine / Zhongguo Zhong xi yi jie he yan jiu hui (chou), Zhong yi yan jiu yuan, zhu ban (CHINA) Mar **1990**, 10 (3) p137-40, 130, ISSN 0254-9034 Journal Code: 8207427
Document type: Journal Article ; English Abstract
Languages: CHINESE
Main Citation Owner: NLM
Record type: Completed
Radioimmunoassay methods were modified for insulin(IRI), C-peptide (IRCP) and **glucagon** (IRG) in the clinical investigation on normal subjects and 38 patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**). In the control group, the peaks of glucose and IRI appeared 1 hour after glucose was taken. IRCP peak, however, appeared 1 hour later. IRG showed its maximum value on fasting and then reached its lowest point at the second hour after glucose loading. The authors' interests were focused on the changes of blood glucose, IRI, IRCP, and IRG in oral glucose tolerance test (OGTT) before and after Ke-Tang-Ling (KTL) was **administered** in **NIDDM**. The results demonstrate that the glucose levels and undercure areas at various phases in OGTT were significantly

decreased (P less than 0.01) in comparison of before and after the **treatment** with KTL in **NIDDM** (including obese and non-obese groups). In non-obese group, however, IRI, IRCP, and their undercure were remarkably increased (P less than 0.01). In obese group their values were decreased. It suggests that KTL plays a therapeutic role in decreasing blood glucose in non-obese **NIDDM** . The mechanism involved in this process may be related to its stimulating effect. IRG levels were decreased also (P less than 0.01) after the **treatment** with KTL in both obese and non-obese **NIDDM**, suggesting an inhibitory effect on **glucagon** secretion from alpha cells in pancrease.

Record Date Created: 19900913
Record Date Completed: 19900913

5/7/186 (Item 25 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08592644 PMID: 2115042

Cytotoxic effects of cytokines on human pancreatic islet cells in monolayer culture.

Rabinovitch A; Sumoski W; Rajotte R V; Warnock G L
Department of Medicine, University of Alberta, Edmonton, Canada.

Journal of clinical endocrinology and metabolism (UNITED STATES) Jul **1990**, 71 (1) p152-6, ISSN 0021-972X Journal Code: 0375362
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Interleukin-1 (IL-1), tumor necrosis factor (TNF), and interferon-gamma (IFN gamma) inhibit insulin release and may be cytotoxic to isolated rodent pancreatic islets. In this study we examined the effects of IL-1, TNF, and IFN gamma on the viability and hormone secretion of islets isolated from adult human pancreas and maintained in monolayer culture. IL-1 and TNF were cytotoxic to the islet cells (20-30% cell lysis) in a 51Cr release cytotoxicity assay, and IFN gamma had only small effects (less than 10% lysis). Combination of maximally cytotoxic concentrations of IL-1 (10 U/mL) and TNF (10(3) U/mL) produced an additive cytotoxic effect. IFN gamma (10(3) U/mL) acted synergistically with IL-1 and TNF, and the three cytokines added together produced maximal islet cell lysis (46.4 +/- 4.3%). Assay of insulin and **glucagon** in the islet monolayers revealed that IL-1, TNF, and IFN gamma inhibited both B- and A-cell secretory functions; however, only IL-1 and TNF produced permanent decreases in insulin and **glucagon** contents in the islet cultures. These findings indicate that IL-1 and TNF, as single agents, are cytotoxic to human islet cells, and that this cytotoxicity can be amplified by combining the cytokines and/or adding IFN gamma. However, the lack of specificity for B-cells in vitro suggests that additional factors might be operative **in vivo** for the cytokine products of macrophages and lymphocytes infiltrating islets to produce the B-cell-specific damage characteristic of type 1 **diabetes**.

Record Date Created: 19900823
Record Date Completed: 19900823

5/7/187 (Item 26 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08469438 PMID: 2697867

Functional capacity of pancreatic B cells in patients with **diabetes** mellitus **type 2** with late true ineffectiveness of sulfonylurea

derivatives]
Sprawnosc czynnosciowa komorek B wysp trzustkowych u chorych na cukrzyce typu 2 z pozna rzeczywista nieskutecznoscia pochodynych sulfonylomocznika.
Kasperska-Czyzykowa T; Jaskolska Ladosz K; Wisniewska K; Galecki A; Nowaczyk R; Woy-Wojciechowski J
Polskie archiwum medycyny wewnetrznej (POLAND) Mar **1989**, 81 (3) p168-75, ISSN 0032-3772 Journal Code: 0401225
Document type: Journal Article ; English Abstract
Languages: POLISH
Main Citation Owner: NLM
Record type: Completed
Fasting concentration of the C peptide in serum was estimated in 150 patients with **type 2 diabetes treated** with insulin because of the late, true ineffectiveness of the sulphonylurea derivatives. In 36 patients selected out of the total group at random the secretion of that peptide was measured after i.v. injection of 1 mg of **glucagon**. Only 9 patients showed trace amounts of that peptide at morning fast (Group A--0.17 +/- 0.08 nmol/l), in 69 the secretion was normal (Sub-Group B1--0.80 +/- 0.25 nmol/l), in 48 moderately elevated (Sub-Group B2--1.67 +/- 0.10 nmol/l) and in 24 markedly elevated (Sub-Group B3--4.54 +/- 2.57 nmol/l). The increments of the peptide C concentration after **glucagon** stimulation were parallel to its fasting concentration, which indicated a proper reactivity of the pancreatic beta-cells in patients with normal or increased basal secretion. The patients with only trace secretion of the peptide C differed from the other by their small, normal body mass and by a longer duration of insulin **treatment**. Very similar insulin needs must be stressed in the patients of the Groups A and B as well as within the Sub-Groups B. In patients with hyperactivity of the beta-cells (Sub-Group B2 and B3) no differences were found, as compared with the other patients, in the prevalence of chronic **diabetes** complications of the micro- or macroangiopathy type, also prevalence of hypertension was equal. The results presented show that in the most patients with **type 2 diabetes** , with the late, true ineffectiveness of the sulphonylurea derivatives the secretory function of the pancreatic islets beta-cells remains normal or is even increased.
Record Date Created: 19900413
Record Date Completed: 19900413

5/7/188 (Item 27 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08447000 PMID: 2407623
Hypoglycemia: still a risk in the elderly.
Walter R M
Internal Medicine, University of California, Davis School of Medicine, Sacramento.
Geriatrics (UNITED STATES) Mar **1990**, 45 (3) p69-71, 74-5, ISSN 0016-867X Journal Code: 2985102R
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hypoglycemia is an underappreciated and potentially fatal complication of insulin and sulfonylurea **treatment** of **diabetes** mellitus in the elderly. After several years of **diabetes**, patients typically lose **glucagon** and epinephrine responses to hypoglycemia, resulting in loss of adrenergic warning symptoms, as well as prolongation of hypoglycemic episodes. Also of pertinence to the elderly, renal disease, liver disease, congestive heart failure, hypothyroidism, hypoadrenalism, medications, and inadequate monitoring may also contribute to hypoglycemia. The benefits of

tight control can be observed only if it is applied to appropriately selected patients. (25 Refs.)
Record Date Created: 19900412
Record Date Completed: 19900412

5/7/189 (Item 28 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08437763 PMID: 2560185
The importance of food and drug plant factors in the combined **treatment** of patients with **type-II diabetes** mellitus]
Znachenie pishchevykh i lekarstvennykh rastitel'nykh faktorov v kompleksnom lechenii bol'nykh sakharnym diabetom II tipa.
Korotkova V D; Perelygina A A; Antsiferov M B; Lobanova A M; Trumpe T E
Problemy endokrinologii (USSR) Nov-Dec **1989**, 35 (6) p24-9, ISSN 0375-9660 Journal Code: 0140673
Document type: Journal Article ; English Abstract
Languages: RUSSIAN
Main Citation Owner: NLM
Record type: Completed
A study was made of the effect of natural (vegetable dish) and refined (food methylcellulose--MC-100 and citrus pectin) vegetable fibers and Arfazetin (antidiabetic species, USSR) on the level of glucose, immunoreactive insulin (IRI), C-peptide, **glucagon** and gastrin in the blood of 41 patients with **type II diabetes** mellitus.
These parameters were investigated on an empty stomach, 1, 2 and 4 h after breakfast I with a standard set of foodstuffs and minimum content of nutritive fibers. Similar investigations were conducted after intake of the same breakfast I in combination with various vegetable components. All the vegetable factors under study were shown to contribute to a decrease in a value of a glycemic rise noted after food intake. A vegetable dish and Arfazetin equally caused a significant rise of IRI secretion and C-peptide 60-90 min. after breakfast. MC-100 and particularly pectin decreased IRI and C-peptide secretion. There was a significant rise of gastrin secretion 1, 2 and 4 h when pectin was added to breakfast. When Arfazetin, a vegetable dish and MC-100 were added to breakfast I, a tendency to a rise of serum gastrin was observed 1 h after breakfast. The level of IRG during investigations with vegetable components did not differ from the results of investigations without these components.
Record Date Created: 19900327
Record Date Completed: 19900327

5/7/190 (Item 29 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08214249 PMID: 2502368
Usefulness of anaerobic threshold in estimating intensity of exercise for diabetics.
Kawaji K; Fujita Y; Yajima Y; Shirataka M; Kubo H
Department of Internal Medicine, School of Medicine, Kitasato University, Kanagawa, Japan.
Diabetes research and clinical practice (NETHERLANDS) May 15 **1989**, 6 (4) p303-9, ISSN 0168-8227 Journal Code: 8508335
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

We examined the utility of the anaerobic threshold (AT) for quantifying the intensity of exercise that a diabetic patient is capable of handling. Thirteen diabetic patients **treated** with buformin exercised on a bicycle ergometer, and comparison was made with 20 healthy subjects matched for age and sex. The AT was determined from VO2 and VE with a personal computer. The intensity of exercise at the AT was 93 +/- 6 W in diabetic men and 80 +/- 10 W in diabetic women, values that were less than those of healthy subjects (P less than 0.05). There was a negative correlation between the intensity of exercise at the AT and the plasma concentration of buformin (P less than 0.01). There were no significant differences in either plasma lactic acid or pyruvic acid concentration at the AT between healthy subjects and diabetics. The plasma glucose at the AT or after exercise was lower than the baseline values in all subjects (P less than 0.01). The plasma insulin at the AT was lower than the baseline values in healthy subjects (P less than 0.01), but not in diabetics. There were no changes in plasma **glucagon** in any group. We concluded that determination of the AT is a simple, non-invasive procedure useful for ascertaining the optimal intensity of exercise for diabetics.

Record Date Created: 19890829

Record Date Completed: 19890829

5/7/191 (Item 30 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08189554 PMID: 2662695

Dietary magnesium supplements improve B-cell response to glucose and arginine in elderly non-insulin dependent diabetic subjects.

Paolisso G; Passariello N; Pizza G; Marrazzo G; Giunta R; Sgambato S; Varricchio M; D'Onofrio F

Institute di Gerontalogia e Geriateria, Napoli, Italy.

Acta endocrinologica (DENMARK) Jul **1989**, 121 (1) p16-20, ISSN 0001-5598 Journal Code: 0370312

Document type: Clinical Trial; Controlled Clinical Trial; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Hypomagnesemia and low erythrocyte magnesium content are both common findings in non-insulin-dependent diabetic subjects. Moreover, intracellular magnesium may play a crucial role in modulating B-cell response to glucose by interfering with potassium permeability. Eight elderly, moderately obese, non-insulin-dependent diabetic subjects were **treated** with either magnesium supplementation (3 g/day) to the diet or placebo. Both **treatment** schemes lasted 4-weeks and were separated by a 'wash-out' of 3 weeks. At the end of each **treatment** period, in glucose test (0.33 g/kg for 3 min) and an iv arginine (5 g) test were performed to determine the B-and A-cell responses. Dietary magnesium supplementation vs placebo produced a slight but significant decrease in basal plasma glucose (8.6 +/- 0.3 vs 8.0 +/- 0.1 mmol/l, p less than 0.05) and an increase in acute insulin response after iv glucose (3.7 +/- 2.3 vs - 14.7 +/- 0.9 pmol.l 1. (10 min)-1, p less than 0.01) and after iv arginine (151 +/- vs 81 +/- 15 pmol.l-1. (10 min)-1, p less than 0.01), respectively. Plasma **glucagon** levels were unaffected by chronic dietary magnesium supplementation as well under basal conditions as in response to arginine. Net increase in acute insulin response after iv glucose and after iv arginine was significantly correlated to the net increase in erythrocyte magnesium content after dietary magnesium supplementation. We conclude that magnesium administration may be a useful adjuvant to the classic hypoglycemic agents in the **treatment** of non-insulin-dependent diabetic subjects.

Record Date Created: 19890808

Record Date Completed: 19890808

5/7/192 (Item 31 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08187701 PMID: 2662383
Metabolic effect of islet B-cell function in insulin-**treated diabetes**.
Gjessing H J; Matzen L E; Iversen S; Faber O K; Froland A
Medical Department, Fredericia Hospital, Denmark.
Scandinavian journal of clinical and laboratory investigation (ENGLAND) Jun **1989**, 49 (4) p337-43, ISSN 0036-5513 Journal Code: 0404375
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We studied the relationship between endogenous insulin secretion and fasting levels of plasma free fatty acids (FFA), plasma acetoacetate plus plasma 3-hydroxybutyrate (total ketone bodies), blood glucose, and HbA1 in 132 diabetic outpatients **treated** with conventional insulin regimens. Patients were divided into four groups according to plasma C-peptide concentration after intravenous stimulation with **glucagon**: one group with C-peptide stimulation less than 0.06 nmol/l, one group with C-peptide stimulation 0.06- less than 0.32 nmol/l, one group with C-peptide stimulation 0.32- less than 0.60 nmol/l, and one group with C-peptide stimulation greater than 0.60 nmol/l. According to clinical criteria the prevalence of insulin-dependent **diabetes** mellitus was approximately 90% in patients with C-peptide stimulation less than 0.32 nmol/l, approximately 25% in patients with C-peptide stimulation from 0.32- less than 0.60 nmol/l, and approximately 10% in patients with C-peptide stimulation greater than 0.60 nmol/l. All metabolic variables were significantly higher in patients without detectable C-peptide in plasma when compared to values found in patients with C-peptide stimulation from 0.06- less than 0.32 nmol/l. These two patient groups also had similar peripheral plasma free insulin levels and were comparable according to age, sex, and body mass index.(ABSTRACT TRUNCATED AT 250 WORDS)
Record Date Created: 19890810
Record Date Completed: 19890810

5/7/193 (Item 32 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08133825 PMID: 2718503
Diabetogenic effect of nifedipine.
Heyman S N; Heyman A; Halperin I
Hadassah University Hospital, Mt. Scopus, Jerusalem, Israel.
DICP - the annals of pharmacotherapy (UNITED STATES) Mar **1989**, 23 (3) p236-7, ISSN 1042-9611 Journal Code: 8904338
Document type: Case Reports; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
This case report describes a 60-year-old diabetic patient whose daily insulin requirements increased by 30 percent following nifedipine administration. **Glucagon** and intravenous glucose tolerance tests were performed with and without nifedipine **treatment**, in order to evaluate the roles of decreased pancreatic beta islet cell function and augmented insulin peripheral resistance in the diabetogenic effect of nifedipine.

Insulin and calculated glucose peripheral utilization extrapolated from the glucose concentration curves were not significantly different. C-peptide levels tended to be lower with nifedipine **treatment** at baseline and during the **glucagon** tests. This may suggest that the altered glycemic control associated with nifedipine was mediated by a suppressed islet beta cell function. The effect of calcium channel-blockers upon glycemic control and the possible mechanisms involved are discussed.
Record Date Created: 19890613
Record Date Completed: 19890613

5/7/194 (Item 33 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08028839 PMID: 2492963
Effects of basal insulin supplementation on disposition of mixed meal in obese patients with **NIDDM**.
McMahon M; Marsh H M; Rizza R A
Department of Medicine, Mayo Clinic and Foundation, Rochester, MN 55905.
Diabetes (UNITED STATES) Mar **1989**, 38 (3) p291-303, ISSN 0012-1797 Journal Code: 0372763
Contract/Grant No.: AM-29953; AM; NIADDK; RR-00585; RR; NCRR
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Basal insulin supplementation has been used as a therapy for patients with non-insulin-dependent **diabetes** mellitus (**NIDDM**) who require insulin. To determine whether basal insulin supplementation in addition to lowering postabsorptive plasma glucose concentration also improves the postprandial pattern of glucose disposition, glucose metabolism after ingestion of a solid mixed meal was assessed in obese patients with **NIDDM** before and after **treatment** with ultralente and compared with glucose metabolism observed in nondiabetic subjects. Splanchnic uptake of ingested glucose clearance was assessed by including [2-3H]glucose (a tracer that only minimally cycles through glycogen) in a solid mixed meal. Postprandial gluconeogenesis was estimated by measuring the rate of incorporation of carbon dioxide into glucose. Net glucose and lipid oxidation were measured by indirect calorimetry. Both splanchnic uptake of ingested glucose (27 +/- 1 vs. 14 +/- 2 g) and postprandial hepatic glucose release (51 +/- 5 vs. 24 +/- 3 g) were greater (P less than .001) in diabetic than in nondiabetic subjects. Although the percentage of postprandial hepatic glucose release accounted for by glucose synthesis from bicarbonate was similar in the two groups (25 +/- 2 vs. 35 +/- 5%), the absolute rate was greater in the diabetic patients (13 +/- 1 vs. 8 +/- 1 g; P less than .05). Postprandial glucose oxidation and glucose disposal (measured either isotopically or by the forearm-catheterization technique) were similar in both groups. However, total lipid oxidation was increased in the diabetic patients. (P less than .05). Two weeks of basal insulin supplementation lowered fasting glucose concentrations (from 219 +/- 22 to 144 +/- 21 mg/dl; P less than .01) and integrated postprandial glycemic response (from 814 +/- 68 to 621 +/- 72 min.mg.ml-1) but not to normal. Although circulating insulin concentrations were two- to threefold greater (P less than .02) after 3 mo of basal insulin supplementation, the postprandial pattern of glucose metabolism remained essentially the same. Basal insulin supplementation decreased (P less than .05) both splanchnic uptake of ingested glucose and hepatic glucose release. The addition of a preprandial injection of soluble insulin to basal insulin supplementation further suppressed (P less than .05) postprandial hepatic glucose release, thereby further improving postprandial glucose tolerance. These studies indicate that initial splanchnic glucose clearance, hepatic glucose

release, and new glucose synthesis, as well as extrahepatic substrate metabolism, are altered in **NIDDM** after ingestion of a mixed meal.(ABSTRACT TRUNCATED AT 400 WORDS)
Record Date Created: 19890404
Record Date Completed: 19890404

5/7/195 (Item 34 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07987239 PMID: 2521365
Morphometrical and biochemical differences of endocrine pancreata between spontaneously hypertensive and normotensive rats with or without neonatal streptozotocin-induced **diabetes**.
Iwase M; Nunoi K; Kikuchi M; Maki Y; Kodama T; Sadoshima S; Fujishima M
Second Department of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka, Japan.
Laboratory investigation; a journal of technical methods and pathology (UNITED STATES) Jan **1989**, 60 (1) p102-5, ISSN 0023-6837
Journal Code: 0376617
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We studied the morphometrical and biochemical changes of endocrine pancreata in spontaneously hypertensive rats (SHR) and normotensive Wistar Kyoto rats (WKY) with or without noninsulin-dependent **diabetes** mellitus induced by neonatal streptozotocin (STZ) **treatment** at 4 months of age. Female (2-day-old) neonates were intraperitoneally injected with 62.5 or 75.0 mg/kg of STZ for SHR, 87.5 or 100.0 mg/kg of STZ for WKY, and vehicle for control. In STZ-**treated** groups, overt hyperglycemia developed in SHR with significantly decreased serum immunoreactive insulin (IRI), whereas in WKY, hyperglycemia was very mild and serum IRI was not lowered. The number and mean size of pancreatic islets did not differ between SHR and WKY, although mean islet size was reduced by half in both compared with that in the corresponding control, respectively. Percentage distribution of insulin-positive B cells in the islet was significantly reduced more in SHR than in WKY (34% of control versus 64% of control, p less than 0.05). Furthermore, pancreatic IRI content was far more reduced in SHR than in WKY (3% of control versus 43% of control, p less than 0.001). In vehicle-**treated** groups, the glycemic levels and the morphometrical islets did not differ between SHR and WKY. However, serum IRI was significantly lower but pancreatic IRI content was higher in SHR than in WKY. The mechanisms of strain differences between SHR and WKY seen in the present study were discussed.
Record Date Created: 19890217
Record Date Completed: 19890217

5/7/196 (Item 35 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07944625 PMID: 3056759
Lilly lecture 1988. Glucose counterregulation and its impact on **diabetes** mellitus.
Gerich J E
University of Pittsburgh School of Medicine, Clinical Research Center, Pennsylvania 15261.
Diabetes (UNITED STATES) Dec **1988**, 37 (12) p1608-17, ISSN 0012-1797 Journal Code: 0372763

Contract/Grant No.: AM-20411; AM; NIADDK
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Glucose counterregulation is the sum of processes that protect against development of hypoglycemia and that restore euglycemia if hypoglycemia should occur. In order of importance, the key counterregulatory factors are **glucagon**, epinephrine, growth hormone, cortisol, and hepatic autoregulation. These act primarily by increasing hepatic glucose output, initially via breakdown of glycogen and later by gluconeogenesis. In people without **diabetes** and in people with **type II** (non-insulin-dependent) **diabetes**, suppression of endogenous insulin secretion during hypoglycemia is also important in permitting full expression of the effects of counterregulation. People with **diabetes** are more prone to develop hypoglycemia for various reasons (e.g., insulin overdose, skipped meals, and intensive exercise); one that has recently been identified is impaired glucose counterregulation: patients with type I (insulin-dependent) **diabetes** (and to a lesser extent, patients with **type II diabetes**) lose the **glucagon** response to hypoglycemia; subsequent development of autonomic neuropathy with concomitant loss of the epinephrine response leads to almost complete paralysis of counterregulation and loss of recognition of hypoglycemia. To make matters worse, an episode of hypoglycemia that causes activation of counterregulation can lead to rebound hyperglycemia (Somogyi phenomenon); if this is improperly **treated**, brittle **diabetes** may follow. Thus, abnormalities in glucose counterregulation may predispose to severe hypoglycemia and prevent achievement of optimal glycemic control in patients with **diabetes**. (115 Refs.)
Record Date Created: 19881227
Record Date Completed: 19881227

5/7/197 (Item 36 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07935090 PMID: 3187231
Postglucagon evolution of blood glucose, a test for **treatment** stabilization and prognosis in **diabetes** mellitus]
Evolutia glicemiei postglucagonice, test pentru stabilirea tratamentului si prognosticului in diabetul zaharat.
Tacu V; Blum M; Tudor G; Dumitriu I; Dinu A; Nastasa V; Ababei V
Revista medico-chirurgicala a Societatii de Medici si Naturalisti din Iasi (ROMANIA) Apr-Jun **1988**, 92 (2) p247-51, ISSN 0300-8738
Journal Code: 0413735
Document type: Journal Article ; English Abstract
Languages: ROMANIAN
Main Citation Owner: NLM
Record type: Completed
Record Date Created: 19881222
Record Date Completed: 19881222

5/7/198 (Item 37 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07848257 PMID: 3042307
Glucagon -stimulated and postprandial plasma C-peptide values as measures of insulin secretory capacity.
Koskinen P J; Viikari J S; Irjala K M

Central Laboratory, University Central Hospital of Turku, Finland.
Diabetes care (UNITED STATES) Apr **1988**, 11 (4) p318-22, ISSN 0149-5992 Journal Code: 7805975
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Basal, postprandial (2 h after breakfast), and **glucagon**-stimulated plasma C-peptide concentrations were determined in a group of 36 adult diabetic patients. Basal and postprandial C-peptide values were measured on consecutive days to estimate the degree of variation of C-peptide secretion. In a subgroup of 15 diabetic patients **treated** chronically with diet and oral hypoglycemic agents (sulfonylureas or a combination of sulfonylureas and metformin), we studied whether administration of sulfonylureas immediately before breakfast had any effect on postprandial C-peptide values. Absolute differences between two consecutive fasting C-peptide concentrations in insulin-requiring patients were less than 0.1 nM in all but 1 patient, in whom the difference was 0.18 nM. In subjects **treated** with oral hypoglycemic agents the median difference was 0.12 nM (range 0-0.38 nM). Absolute differences between two consecutive postprandial C-peptide concentrations were all less than 0.1 nM in insulin-requiring patients. No significant difference was found between postprandial C-peptide concentrations with or without preceding administration of oral hypoglycemic agents (medians 1.35 and 1.30 nM, respectively). **Glucagon** -stimulated C-peptide concentrations were somewhat higher than the postprandial values. However, equal discrimination between insulin-requiring and non-insulin-requiring diabetic patients was found by measuring postprandial or **glucagon**-stimulated C-peptide concentrations.

Record Date Created: 19880922
Record Date Completed: 19880922

5/7/199 (Item 38 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07823216 PMID: 2968880

Insulin requirement in non-insulin-dependent **diabetes** mellitus: relation to simple tests of islet B-cell function and insulin sensitivity.

Gjessing H J; Matzen L E; Pedersen P C; Faber O K; Froland A
Medical Department, Fredericia Hospital, Denmark.

Diabetic medicine - a journal of the British Diabetic Association (ENGLAND) May-Jun **1988**, 5 (4) p328-32, ISSN 0742-3071 Journal Code: 8500858
Erratum in Diabetic Med 1988 Jul-Aug;5(5) 422
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Evaluation of simple tests of islet B-cell function and insulin sensitivity as predictors of metabolic control was performed during 3 months of insulin withdrawal in 25 insulin-**treated** diabetic subjects. All patients had a **glucagon** stimulated plasma C-peptide concentration above 0.33 nmol/l and a fasting plasma C-peptide concentration above 0.20 nmol/l a few days before insulin withdrawal. Insulin sensitivity was measured as the glucose disappearance rate (k) during an intravenous insulin tolerance test. Two patients were considered insulin-requiring due to high fasting blood glucose levels (greater than 20 mmol/l) and two patients due to an increase in glycosylated haemoglobin of more than 1.1% (greater than approximately 3SD) in combination with weight loss. None of the remaining patients had a significant increase in glycosylated

haemoglobin. An inverse correlation was found between stimulated C-peptide levels and insulin sensitivity (r = 0.41, p less than 0.05). Fasting and stimulated C-peptide concentrations of 0.40 and 0.70 nmol/l, respectively, separated non-insulin-requiring patients from a group consisting of both insulin- and non-insulin-requiring patients. At these C-peptide levels the predictive value of a positive test was 100% while the predictive value of a negative test was as low as 33% or 27% depending on whether fasting or stimulated C-peptide concentration was used. Including the k value in the prediction only increased the predictive values of negative tests to 40% and 33%, respectively.
Record Date Created: 19880818
Record Date Completed: 19880818

5/7/200 (Item 39 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07808583 PMID: 2898427
Postprandial glycaemic effects of a long-acting somatostatin analogue (octreotide) in non-insulin dependent **diabetes** mellitus.
Williams G; Fuessl H S; Burrin J M; Chilvers E; Bloom S R
Department of Medicine, Royal Postgraduate Medical School, London, England.
Hormone and metabolic research. Hormon- und Stoffwechselforschung. Hormones et metabolisme (GERMANY, WEST) Mar **1988**, 20 (3) p168-70 , ISSN 0018-5043 Journal Code: 0177722
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Postprandial changes in blood glucose, insulin and **glucagon** were examined in 7 non-insulin dependent diabetic patients, before and after 3 days' **treatment** with the somatostatin analogue, octreotide (50 ug injected subcutaneously thricedaily). After octreotide injection, postprandial rises in plasma insulin and **glucagon** were significantly flattened. The postprandial glycaemic rise was delayed but the area under the glycaemic curve was not increased. Animal studies have suggested that octreotide inhibits growth hormone and **glucagon** secretion much more powerfully than native somatostatin, while relatively sparing insulin secretion. However, the present findings suggest that this analogue is not sufficiently selective to be therapeutically useful in non-insulin dependent **diabetes**.
Record Date Created: 19880804
Record Date Completed: 19880804

5/7/201 (Item 40 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07777649 PMID: 2897272
Impaired exocrine pancreatic function in diabetics with diarrhea and peripheral neuropathy.
el Newihi H; Dooley C P; Saad C; Staples J; Zeidler A; Valenzuela J E
Department of Medicine, USC School of Medicine, Los Angeles 90033.
Digestive diseases and sciences (UNITED STATES) Jun **1988**, 33 (6) p705-10, ISSN 0163-2116 Journal Code: 7902782
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Exocrine pancreatic insufficiency has been observed in some diabetics with peripheral neuropathy and diarrhea. Several mechanisms may be responsible for this insufficiency: (1) pancreatic atrophy, (2) disruption of the cholinergic enteropancreatic reflexes, or (3) elevated serum levels of peptides such as **glucagon** and pancreatic polypeptide which are known to inhibit pancreatic exocrine secretion. To clarify the mechanism(s) involved in this exocrine pancreatic impairment, we studied 10 diabetics with diarrhea and peripheral neuropathy. Their results were compared to those of eight normal volunteers. Each subject underwent a standardized pancreatic function study which assessed nonstimulated secretion, the response to intrajejunal infusion of a mixture of amino acids, and the output following intravenous administration of secretin and cholecystokinin (CCK). In separate studies, the effect of a background infusion of bethanechol and secretin on the pancreatic response to CCK was assessed in six patients and six normal controls. Compared to normals, all diabetics exhibited a significant reduction in both enzyme and bicarbonate secretion to all stimuli. This reduction was not corrected by **administering** bethanechol. Plasma **glucagon** and pancreatic polypeptide levels in diabetics were not significantly higher than those in controls. We conclude that diabetics with diarrhea and peripheral neuropathy exhibit impairment of their exocrine pancreatic secretion and possible mechanisms for this are discussed.

Record Date Created: 19880707
Record Date Completed: 19880707

5/7/202 (Item 41 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07774813 PMID: 3285822

Atherosclerotic vascular disease in middle-aged, insulin-**treated**, diabetic patients. Association with endogenous insulin secretion capacity.

Ronnemaa T; Laakso M; Puukka P; Kallio V; Pyorala K
Rehabilitation Research Centre, Social Insurance Institution, Turku, Finland.

Arteriosclerosis (Dallas, Tex.) (UNITED STATES) May-Jun **1988**, 8 (3) p237-44, ISSN 0276-5047 Journal Code: 8401388
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The prevalence of atherosclerotic vascular disease (ASVD) and its risk factors were investigated in 263 insulin-**treated** diabetic patients, ages 45 to 64 years, who were older than 30 years when their **diabetes** was diagnosed. The patients were divided into two groups based on the degree of endogenous insulin secretion capacity: Group A: **glucagon** -stimulated plasma C-peptide less than 0.20 nmol/l and Group B: C-peptide greater than or equal to 0.20 nmol/l. The age-adjusted prevalence of definite myocardial infarction was significantly higher in Group B than in Group A (16.8% vs. 5.2%, p less than 0.01). A similar difference between Groups A and B was found for definite or possible coronary heart disease (54.6% vs. 32.9%, p less than 0.001) and stroke (9.3% vs. 2.0%, p less than 0.05). In multivariate analysis, high **glucagon**-stimulated plasma C-peptide level (greater than or equal to 0.20 nmol/l) was positively associated with definite or possible coronary heart disease independently of other cardiovascular risk factors. Our results indicate that among insulin-**treated** patients with a late onset of **diabetes**, the prevalence of ASVD is markedly higher in those with persistent endogenous insulin secretion (noninsulin-dependent **diabetes**) than in those with low or no insulin secretion (insulin-dependent **diabetes**).

Record Date Created: 19880621

Record Date Completed: 19880621

5/7/203 (Item 42 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07750119 PMID: 3282943
Counterregulatory hormone responses preserved after long-term intravenous insulin infusion compared to continuous subcutaneous insulin infusion.
Gulan M; Perlman K; Sole M; Albisser A M; Zinman B
Division of Endocrinology and Metabolism, Toronto General Hospital, Ontario, Canada.
Diabetes (UNITED STATES) May **1988**, 37 (5) p526-31, ISSN 0012-1797 Journal Code: 0372763
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The counterregulatory hormone responses of cortisol, growth hormone, **glucagon** , epinephrine, norepinephrine, and dopamine to a fixed hypoglycemic stimulus (50 mg/dl for 1 h) were studied in five type I (insulin-dependent) diabetic subjects during conventional insulin therapy (CT), after 3 mo of continuous subcutaneous insulin infusion (SC), and after 3 mo of continuous intravenous insulin infusion (IV). During the two infusion periods, the overall mean levels of preprandial blood glucose (116 +/- 6 SC vs. 114 +/- 5 mg/dl IV) and glycosylated hemoglobin (6.1 +/- 2 SC vs. 5.9 +/- 2% IV) were virtually identical, but there were more hypoglycemic episodes and greater variability of preprandial blood glucose levels during SC than with IV. During the last 30 min of the hypoglycemic clamps, the mean levels of epinephrine and cortisol were significantly lower after 3 mo of SC (epinephrine, 268 +/- 80 pg/ml; cortisol, 14 +/- 1 microgram/dl) than with both CT (epinephrine 485 +/- 80 pg/ml; cortisol, 20 +/- 2 micrograms/dl) and IV (epinephrine, 443 +/- 62 pg/ml; cortisol, 19 +/- 2 micrograms/dl)(P less than .05). The mean growth hormone level was significantly (P less than .05) lower after SC (37 +/- 9 ng/ml) than after IV (79 +/- 12 ng/ml), but it did not reach statistical significance compared with CT (66 +/- 12 ng/ml). The mean **glucagon**, dopamine, and norepinephrine levels during the same period of hypoglycemia were not different when all **treatment** regimens were compared. We conclude that intensified insulin therapy with SC leads to significant blunting of the counterregulatory hormone response to hypoglycemia, whereas IV does not.(ABSTRACT TRUNCATED AT 250 WORDS)
Record Date Created: 19880601
Record Date Completed: 19880601

5/7/204 (Item 43 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07749413 PMID: 3129276
[Insulin therapy of obese diabetic patients? Consequences for the evaluation of insulin secretion and metabolic behavior]
Insulintherapie bei fettsuchtigen Diabetikern? Konsequenzen aus der Bewertung des Insulinsekretions- und Stoffwechselverhaltens.
Verlohren H J; Danneberg G; Brunner E; Pohl A; Bierwolf B
Deutsche Zeitschrift fur Verdauungs- und Stoffwechselkrankheiten (GERMANY, EAST) **1987**, 47 (6) p311-25, ISSN 0012-1053 Journal Code: 0372760
Document type: Journal Article ; English Abstract
Languages: GERMAN

Main Citation Owner: NLM
Record type: Completed
In 83 diabetics insulin secretion was examined after a mean **diabetes** duration of 7.5 years, when an insufficient metabolic situation could be found. Insulin secretion was stimulated with 100 g glucose (orally) and 1.0 mg **glucagon** i.v. (60 min after glucose intake). We investigated additionally in a retrospective manner blood-glucose and urine glucose behaviour as well as the development of the body weight. In dependence of the actual body weight at the time of investigation of insulin secretion, two groups were formed: b. w. less than 120% acc. Broca index, group A, n = 38; b. w. greater than 120% acc. Broca index. group B, n = 45). Immediately after manifestation of the disease 71 **diabetes** were **treated** with pure dietetic measures. At the examination of insulin secretion all patients were **treated** with glibenclamide. After this examination in 20 patients of the group A and in 17 patients of the group B an insulinisation was started. In the others glibenclamide **treatment** was continued. The general characteristics of the whole group was a significant reduction of the maximum stimulability of insulin secretion, compared with the insulin secretion of n = 19 healthy probands (11 probands with normal body weight and 8 obese probands). A hyperinsulinism (maximum values higher than mean + 1 s of the health persons) could not be found in any case. The mean of the maximum insulin values was below mean - 1 s of the healthy persons. Insulinisation provoked an improvement of the metabolic situation. This was correlated with an additional improvement of the subjective behaviour. Conclusion: Evaluation of insulin secretion in obese diabetics with bad metabolic situation is necessary to find out those who are to be **treated** with insulin. We have no clinical or other possibilities to recognize patients with a hyperinsulinism or reduced insulin secretion than by evaluation of insulin secretion alone. But higher degrees of decompensated metabolism are nearly always explained by a significant reduction of insulin secretion.
Record Date Created: 19880527
Record Date Completed: 19880527

5/7/205 (Item 44 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07742643 PMID: 2965784
Biochemical changes in rhesus monkey during the first days after streptozotocin administration are indicative of selective beta cell destruction.
Takimoto G; Jones C; Lands W; Bauman A; Jeffrey J; Jonasson O
Department of Surgery, University of Illinois College of Medicine, Chicago.
Metabolism- clinical and experimental (UNITED STATES) Apr **1988**, 37 (4) p364-70, ISSN 0026-0495 Journal Code: 0375267
Contract/Grant No.: AM18284; AM; NIADDK
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Hormonal and glycemic changes in 22 rhesus monkeys were characterized during the first days after **treatment** with streptozotocin (STZ) (45 to 55 mg/kg, **administered** intravenously [IV]). Almost half (10/22) of the monkeys developed insulin-dependent **diabetes** mellitus (STZ-IDDM) within five days following injection. Four of the remaining monkeys did not become insulin dependent for at least 6 months after STZ **treatment**, during which time they were considered non-insulin-dependent, and eight monkeys never required exogenous insulin. In the STZ-IDDM group, plasma immunoreactive c-peptide (IRC-P) levels fell by three hours after STZ from

a mean +/- SEM of 252 +/- 82 to 101 +/- 45 pg/mL, as glucose and immunoreactive **glucagon** (IRG) levels increased from 65 +/- 3 and 120 +/- 37, respectively, to 336 +/- 43 mg/dL and 234 +/- 52 pg/mL, respectively. Between six and 30 hours after **treatment** , IRC-P increased to a peak of 1,561 +/- 360 pg/mL before falling permanently to less than 60 pg/mL by 66 hours. During this period, glucose and IRG responded in a reciprocal fashion by falling and then increasing to levels above 300 mg/dL and 300 pg/mL, respectively, by 66 hours. In the non-insulin-dependent **diabetes** mellitus (STZ-**NIDDM**) group, no clear reciprocal relationship between IRC-P and glucose and IRG was obtained. In nine additional monkeys subjected to total pancreatectomy (Px), IRC-P and IRG levels fell immediately and permanently by greater than 90% and 75%, respectively. Levels of immunoreactive somatostatin increased steadily over the initial 96 hours following STZ, but did so both STZ-IDDM and Px monkey groups.(ABSTRACT TRUNCATED AT 250 WORDS)

Record Date Created: 19880523

Record Date Completed: 19880523

5/7/206 (Item 45 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07723869 PMID: 3127418

Effect of a sulfonylurea and insulin on energy expenditure in **type II diabetes** mellitus.

Welle S; Nair K S; Lockwood D

Endocrine-Metabolism Unit, University of Rochester, New York 14603.

Journal of clinical endocrinology and metabolism (UNITED STATES) Mar **1988**, 66 (3) p593-7, ISSN 0021-972X Journal Code: 0375362

Contract/Grant No.: AM-20494; AM; NIADDK; RR-00044; RR; NCRR

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Previous studies demonstrated that administration of insulin and oral hypoglycemic agents tends to produce weight gain in **type II** diabetic patients. The goal of this study was to determine the potential contribution of changes in metabolic rate and urinary glucose excretion to changes in energy balance associated with **treatment** with glyburide and insulin. Six obese **type II** diabetic patients (52-61 yr old; 123-214% of ideal weight) were fed a weight-maintaining diet of fixed composition and caloric content in a Clinical Research Center. The mean fasting plasma glucose concentrations were 10.7 +/- 1.3 (+/- SE) mmol/L before **treatment** , 7.9 +/- 1.4 mmol/L at the end of 2 weeks of glyburide **treatment**, and 5.2 +/- 0.3 mmol/L at the end of 2 weeks of insulin **treatment**. Urinary glucose excretion decreased from 48 +/- 19 g/day before **treatment** to 20 +/- 9 g/day at the end of glyburide **treatment** and 2 +/- 1 g/day at the end of insulin **treatment**. Neither **treatment** affected mean postabsorptive resting metabolic rate (untreated 4.86 +/- 0.50 kJ/min; glyburide-**treated**, 4.63 +/- 0.45 kJ/min; insulin-**treated** , 4.70 +/- 0.46 kJ/min) or postprandial resting metabolic rate (untreated, 5.71 +/- 0.55 kJ/min; glyburide-**treated**, 5.60 +/- 0.39 kJ/min; insulin-**treated**, 5.70 +/- 0.51 kJ/min). However, the two patients with the largest decreases in urinary glucose excretion also had decreases in energy expenditure. These data indicate that many obese **type II** diabetic patients could have significant weight gain from reduced energy losses alone.

Record Date Created: 19880512

Record Date Completed: 19880512

5/7/207 (Item 46 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07714822 PMID: 3279723
Stopping insulin **treatment** in middle-aged diabetic patients with high postglucagon plasma C-peptide. Effect on glycaemic control, serum lipids and lipoproteins.
Laakso M; Sarlund H; Korhonen T; Voutilainen E; Majander H; Hakala P; Uusitupa M; Pyorala K
Department of Medicine, Kuopio University Central Hospital, Finland.
Acta medica Scandinavica (SWEDEN) **1988**, 223 (1) p61-8, ISSN 0001-6101 Journal Code: 0370330
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We studied the successfulness of stopping insulin **treatment** in middle-aged diabetic patients aged 45-64 with a high postglucagon C-peptide level and the effects of this change on glycaemic control, serum lipids and lipoproteins. Insulin **treatment** was successfully stopped in 15 of our 22 patients who satisfied the inclusion criteria for the study and were selected on the basis of a computer file including practically all diabetic patients **treated** with insulin in the Kuopio University Central Hospital region (population base 250,000 inhabitants). Insulin therapy was restarted in seven patients during the first 3 months after discharge. During the following 9 months insulin therapy was restarted in another three patients so that after a 1-year follow-up period half of the diabetic patients whose insulin therapy was stopped had been switched back to insulin. Insulin therapy was seldom successfully stopped if the postglucagon C-peptide value was under the limit of 1.0 nmol/l. Glycaemic control did not change during the follow-up, although there was a significant weight loss in diabetic patients. No changes were observed in serum lipids or lipoproteins with the exception of LDL cholesterol, which showed a significant reduction during the 3-month follow-up. In conclusion, insulin therapy can often be successfully stopped in patients with postglucagon C-peptide over the limit of 1.0 nmol/l without worsening of glycaemic control and without unfavourable changes in serum lipid and lipoprotein levels.
Record Date Created: 19880421
Record Date Completed: 19880421

5/7/208 (Item 47 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07664601 PMID: 3123115
Serum C-peptide after 6 months on glibenclamide remains higher than during insulin **treatment**.
Peacock I; Watts R; Selby C; Tattersall R B
University Hospital, Nottingham, UK.
Diabetes research (Edinburgh, Lothian) (SCOTLAND) Oct **1987**, 6 (2) p57-9, ISSN 0265-5985 Journal Code: 8502339
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Serum C-peptide was measured fasting and 6 minutes after **glucagon** (1 mg given intravenously) in 49 patients with non-insulin-dependent **diabetes** mellitus, after 4 and 6 months of successive periods of

treatment with insulin and oral hypoglycaemics (glibenclamide and metformin), given in random order. Glycaemic control was not significantly different on the two **treatments**, but C-peptide was much higher while the patients were on glibenclamide. We conclude that glibenclamide stimulates pancreatic insulin production even after 6 months **treatment**.
Record Date Created: 19880226
Record Date Completed: 19880226

5/7/209 (Item 48 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07585533 PMID: 3117609
Different effects of glyburide and glipizide on insulin secretion and hepatic glucose production in normal and **NIDDM** subjects.
Groop L; Luzi L; Melander A; Groop P H; Ratheiser K; Simonson D C; DeFronzo R A
Yale University School of Medicine, New Haven, Connecticut.
Diabetes (UNITED STATES) Nov **1987**, 36 (11) p1320-8, ISSN 0012-1797 Journal Code: 0372763
Contract/Grant No.: AM-24092; AM; NIADDK; F05-TW0-3451; TW; FIC; RR125; RR; NCRR
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Glyburide (GB) and glipizide (GZ) differ in their pharmacokinetics, but it is not known whether they also differ in mode of action. To examine this question, 10 young healthy subjects and 6 non-insulin-dependent diabetic (**NIDDM**) patients participated in each of three studies: 1) infusion of saline for 120 min followed by a 100-min hyperglycemic (125 mg/dl) clamp; 2) 120-min primed continuous infusion of GZ followed by a 100-min hyperglycemic clamp; and 3) 120-min primed continuous infusion of GB followed by a 100-min hyperglycemic clamp. The GB and GZ infusions were continued throughout the hyperglycemic clamp. Similar plasma concentrations of GB and GZ were obtained in both groups. All studies were performed with [3-3H]glucose to allow quantification of hepatic glucose production. When **administered** under basal conditions of glycemia, the acute phase (0-10 min) of plasma insulin and C-peptide increase in both control and **NIDDM** subjects was twice as great with GZ compared with GB (P less than .01). During the hyperglycemic-clamp studies performed in normal subjects, both GB and GZ increased the first- (1.6-fold) and second- (2.2-fold) phase plasma insulin responses more than hyperglycemia alone. During the hyperglycemic clamp in **NIDDM** subjects, the first-phase plasma insulin response was absent, and the second-phase insulin response was markedly impaired. Neither GB nor GZ improved first-phase insulin secretion in the **NIDDM** patients. In both **NIDDM** and control subjects, the effects of hyperglycemia and sulfonylurea drugs (both GB and GZ) on the first- and second-phase plasma insulin responses were simply additive.(ABSTRACT TRUNCATED AT 250 WORDS)
Record Date Created: 19871216
Record Date Completed: 19871216

5/7/210 (Item 49 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07583508 PMID: 2959439
Guar sprinkled on food: effect on glycaemic control, plasma lipids and

gut hormones in non-insulin dependent diabetic patients.
Fuessl H S; Williams G; Adrian T E; Bloom S R
Department of Medicine, Royal Postgraduate Medical School, London, UK.
Diabetic medicine - a journal of the British Diabetic Association (ENGLAND) Sep-Oct **1987**, 4 (5) p463-8, ISSN 0742-3071
Journal Code: 8500858
Document type: Clinical Trial; Controlled Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The effects of guar granules sprinkled over food on carbohydrate and lipid metabolism were studied in a double-blind cross-over trial in 18 patients with non-insulin-dependent **diabetes** mellitus (mean +/- SEM age 61.3 +/- 2.5 years). Five-gram guar granules (Guarem, Rybar Laboratories, Amersham, Bucks) were sprinkled over food at each main meal for 4 weeks, and during a 4-week placebo period (separated by a 2-week 'wash-out' period), 5 g wheat bran was taken in the same way. Diabetic **treatment** was not changed during the study. Mean fasting plasma glucose (FPG) concentration and glycosylated haemoglobin (HbA1) concentration after **treatment** were significantly lower than after the placebo period (FPG 8.29 +/- 0.47 vs 8.78 +/- 0.53 mmol/l, p less than 0.05; HbA1: 8.70 +/- 0.39 vs 9.09 +/- 0.39%, p less than 0.05). There was a 50% reduction in the incremental area under the postprandial glycaemic curve when guar was eaten with a standardized test meal. Total plasma cholesterol decreased from 5.79 +/- 0.29 to 5.19 +/- 0.22 mmol/l (p less than 0.05) after the guar **treatment** period. Guar ingestion reduced postprandial insulin and enteroglucagon responses, the latter significantly so, but had no apparent effect on gastric inhibitory polypeptide, pancreatic **glucagon**, gastrin, and pancreatic polypeptide.
Record Date Created: 19871210
Record Date Completed: 19871210

5/7/211 (Item 50 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07575557 PMID: 2889321
Fibre and the diabetic diet. An evaluation of the metabolic response to standardized meals.
Hagander B
Department of Community Health Sciences, University of Lund, Dalby, Sweden.
Acta medica Scandinavica. Supplementum (SWEDEN) **1987**, 716 p1-55 , ISSN 0365-463X Journal Code: 0370331
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Dietary fibre has a beneficial influence on glucose homeostasis, varying for different fibre sources. Fruit, wheat, rye and beet fibre were studied in isoenergetic meals for NIDD patients and healthy volunteers. The effects of extrusion cooking and flaking were also evaluated. The metabolic response was followed by continuous glucose monitoring and by analyses of pancreatic and gastrointestinal hormones as well as plasma lipid concentrations, For NIDD patients the effects, reflected in the area and the shape of the glucose curve, were greater for the more soluble fibre types, but the insulin and C-peptide responses were largely unaffected by dietary fibre. Beet fibre gave increased somatostatin concentrations also in age-matched healthy controls. They showed, however, unchanged plasma glucose responses and markedly decreased insulin and C-peptide levels. These changes were associated with less pronounced postprandial glycerol

reduction, but otherwise none of the fibre preparations affected the postprandial lipemia. Extruded bread, based on wholegrain wheat flour, with high availability of in vitro starch, elicited a greater glucose response than wholegrain wheat bread, associated with a modest increase of GIP and insulin and with a stimulated early **glucagon** secretion. Flaked rye seemed to contain both faster and slower carbohydrates than the corresponding rye bread of similar fibre content. Analyses of the glucose curves suggested that the effect of fibre might be mediated by an effect on glucose absorption and parallel experiments in rat indicated that a delayed rate of gastric emptying might contribute. Further, the liver glycogen content was higher in rats given a slowly absorbed gastric load. A realistic increase in fibre content, given in long-term **treatment,** improved the metabolic control in NIDD patients, by decreasing the fasting blood glucose and LDL-cholesterol levels, as well as the LDL/HDL ratio. Hypothetically, slower absorption achieved with dietary fibre increases the proportion of glycogen in the liver. This postprandial improvement may cause the long-term trend to normalization of the fasting blood glucose level.

Record Date Created: 19871103
Record Date Completed: 19871103

5/7/212 (Item 51 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07558191 PMID: 2888547

Effects of somatostatin analogue SMS 201-995 in non-insulin-dependent **diabetes.**

Davies R R; Miller M; Turner S J; Watson M; McGill A; Orskov H; Alberti K G; Johnston D G

Department of Medicine, Royal Victoria Infirmary, Newcastle upon Tyne, Denmark.

Clinical endocrinology (ENGLAND) Dec **1986,** 25 (6) p739-47,
ISSN 0300-0664 Journal Code: 0346653

Document type: Clinical Trial; Controlled Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The 24-h hormonal and metabolic profiles obtained in five non-insulin-dependent diabetics receiving twice daily s.c. injections of the long-acting somatostatin analogue SMS 201-995 (50 micrograms) have been compared with those obtained following placebo injection. Injections were given 30 min before breakfast and the evening meal. GH secretion was not suppressed by the analogue **administered** in this manner. Despite suppression of serum insulin levels following breakfast and the evening meal, blood glucose levels were similar during the two study periods with no evidence of worsening in diabetic control. Prolonged suppression of plasma **glucagon** levels was observed and the nocturnal elevation in serum TSH levels was abolished. Free T4 levels fell significantly following the analogue but total T3 levels were unaffected. Blood alanine levels were elevated throughout the study period following SMS 201-995 but changes in lactate, pyruvate, glycerol and 3-hydroxybutyrate were minor. All five subjects suffered gastrointestinal side-effects. SMS 201-995 (50 micrograms) given twice daily before meals does not cause a deterioration in metabolic control, does not suppress 24-h GH secretion and causes significant side-effects in patients with non-insulin-dependent **diabetes** mellitus.

Record Date Created: 19871119
Record Date Completed: 19871119

5/7/213 (Item 52 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07543355 PMID: 3306277
Association of serum lipids and lipoproteins with plasma C-peptide concentration in non-insulin-dependent diabetic and non-diabetic subjects.
Sarlund H; Laakso M; Pyorala K; Penttila I
Metabolism- clinical and experimental (UNITED STATES) Sep **1987**, 36 (9) p840-5, ISSN 0026-0495 Journal Code: 0375267
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Serum lipids and lipoproteins were studied in 149 non-insulin-dependent diabetic subjects **treated** with diet or oral drugs (75 men, 74 women) and in 101 nondiabetic control subjects (49 men, 52 women) in relation to endogenous insulin secretion capacity measured by plasma C-peptide response to intravenous **glucagon** . Serum HDL- and HDL2-cholesterol concentrations were lower and VLDL-cholesterol and total and VLDL-triglyceride concentrations higher in subjects with high C-peptide response (above the median) than in subjects with low C-peptide response (lower or equal to median) both in diabetic and control subjects of both sexes. Adjustment for the effect of obesity abolished these differences in serum lipids and lipoproteins in diabetic subjects but not in control subjects. This may indicate that obesity has stronger influence on serum lipids in diabetic subjects than in nondiabetic subjects.
Record Date Created: 19870928
Record Date Completed: 19870928

5/7/214 (Item 53 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07496002 PMID: 3604753
Fasting, postprandial and postprandial plus **glucagon**-stimulated plasma C-peptide levels in non-insulin-dependent diabetics and in control subjects.
Sarlund H; Laakso M; Pyorala K; Penttila I
Acta medica Scandinavica (SWEDEN) **1987**, 221 (4) p377-83, ISSN 0001-6101 Journal Code: 0370330
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We have studied fasting, postprandial and postprandial plus **glucagon** -stimulated plasma C-peptide levels in 149 non-insulin-dependent diabetics **treated** either with diet or oral drugs and in 101 non-diabetic control subjects. Diet-**treated** diabetics showed the highest fasting, postprandial and post-**glucagon** C-peptide levels in both sexes. In men, diabetics **treated** with oral drugs showed lower postprandial and **glucagon**-stimulated C-peptide levels than control subjects, while in women C-peptide levels in this group of diabetics were similar to those in control subjects. The distribution of individual plasma C-peptide levels was wide in non-insulin-dependent diabetics and control subjects and there was considerable overlapping in plasma C-peptide distribution for diabetics and control subjects. Fasting and post-**glucagon** plasma C-peptide levels in diabetics showed an inverse association to plasma glucose levels and a positive association to degree of obesity, but no association with the known duration of **diabetes**.

Record Date Created: 19870805
Record Date Completed: 19870805

5/7/215 (Item 54 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07495120 PMID: 3300063
Presentation of an insulin-**treated** patient group within the scope of a 5-year study of the **Diabetes** Intervention Study (DIS)]
Darstellung der insulinisierten Patientengruppe im Rahmen der Funfjahresuntersuchungen der Diabetesinterventionsstudie (DIS).
Lindner J; Dempe A; Neubert G; Hanefeld M; Haller H
Zeitschrift fur die gesamte innere Medizin und ihre Grenzgebiete (GERMANY, EAST) Apr 1 **1987**, 42 (7) p198-200, ISSN 0044-2542
Journal Code: 21730470R
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial ; English Abstract
Languages: GERMAN
Main Citation Owner: NLM
Record type: Completed
The **diabetes** intervention study (DIS) is an intervention and examination programme which in dietetically conducible diabetics who freshly became manifest shall decrease the incidence of cardiovascular diseases and analyse the influence of various steps of intervention on the course of **diabetes**. In the course of 5 years 54 out of 988 patients were insulinized by reason of deteriorations of metabolism. There were no significant differences between the intervention and control group concerning age, sex, index of ideal weight, fasting blood glucose, quantity of injected insulin and duration of the insulin **treatment**. By means of a C-peptide short-time test following **glucagon** stimulation an attempt of differentiation into type 1 and **type 2** diabetics, was performed and compared with the results in literature.
Record Date Created: 19870812
Record Date Completed: 19870812

5/7/216 (Item 55 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07494878 PMID: 3111096
Possibility of transferring patients with **type-II diabetes** mellitus **treated** with small doses of sulfonylurea preparations to diet therapy]
Vuzmozhnost za preminavane na dietolechenie u bolni sus zakharna bolest tip II, lekuvani s malki dozi sulfonilureini preparati.
Borisova A M; Koev D; Kirilov G
Vutreshni bolesti (BULGARIA) **1987**, 26 (2) p63-8, ISSN 0506-2772 Journal Code: 0032666
Document type: Journal Article ; English Abstract
Languages: BULGARIAN
Main Citation Owner: NLM
Record type: Completed
Nine patients with **diabetes** mellitus, **type II** (6 males and 3 females) were studied. The average duration of the disease was 7.1 years. The patients were perorally **treated** with glibenclamide (5-10 mg daily). Beta-cellular function was studied with **glucagon** as well as the peripheral insulin sensitivity of the patients on the background of the peroral **treatment** and after its two-week discontinuation--on the background of dietetic **treatment** . No significant difference in

beta-cellular function, insulin sensitivity and metabolic compensation was established. Part of the patients with **diabetes** mellitus, **type II, treated** with low and medium doses of glibenclamide, could well be compensated only by an adequate diet.
Record Date Created: 19870731
Record Date Completed: 19870731

5/7/217 (Item 56 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07481103 PMID: 3598035
Exercise and the management of **diabetes** mellitus.
Franz M J
Journal of the American Dietetic Association (UNITED STATES) Jul **1987**, 87 (7) p872-80, ISSN 0002-8223 Journal Code: 7503061
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Fuel metabolism in individuals with well-controlled **diabetes** is similar to that occurring in persons who do not have **diabetes**. During the initial phase of physical exercise, muscle glycogen is the primary source of fuel. As exercise continues, blood glucose and free fatty acids (FFAs) become increasingly important substrates. FFAs become the major fuel source as glucose utilization decreases. Whereas in individuals who do not have **diabetes**, blood glucose levels vary little during exercise, the person with insulin-dependent **diabetes** mellitus (IDDM) may experience an increase in blood glucose, a modest decrease, or a marked decrease, which can result in hypoglycemia. In insulin-**treated** persons with mild hyperglycemia, exercise is accompanied by a fall in blood glucose. In contrast, in persons with marked hyperglycemia and ketosis, exercise may cause a further rise in both blood glucose and ketone levels. The glycemic response to exercise is dependent on the plasma concentration of insulin. Physical training improves glucose tolerance in individuals with noninsulin-dependent **diabetes** mellitus (**NIDDM**); in persons with IDDM, it may diminish insulin requirements. The repletion of muscle and liver glycogen, which takes place for 24 to 48 hours after exercise, requires a minimum amount of insulin in addition to carbohydrate feeding. Persons using insulin may need to increase food intake prior to, during, and after exercise and/or decrease insulin dosage as well. Persons with IDDM can exercise safely, and persons with **NIDDM** can achieve better control by following the guidelines outlined for exercise prescription.
Record Date Created: 19870811
Record Date Completed: 19870811

5/7/218 (Item 57 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07446460 PMID: 3581663
Clinical characteristics in the discrimination between patients with low or high C-peptide level among middle-aged insulin-**treated** diabetics.
Laakso M; Sarlund H; Pyorala K
Diabetes research (Edinburgh, Lothian) (SCOTLAND) Feb **1987**, 4 (2) p95-9, ISSN 0265-5985 Journal Code: 8502339
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

We compared sensitivity, specificity and accuracy of selected clinical characteristics (age at diagnosis, initiation of permanent insulin therapy from diagnosis and degree of obesity) in the discrimination between diabetics with low or high fasting or post-**glucagon** C-peptide level in a population of 171 middle-aged insulin-**treated** diabetics (81 men, 90 women) living in East Finland. Individual clinical criteria were poor discriminators alone but their combinations gave high specificity for the low and high fasting and post-**glucagon** C-peptide classes. The specificity and the accuracy of combined criteria seemed to be somewhat higher among male than among female insulin-**treated** diabetics. The association between clinical characteristics and fasting or postglucagon C-peptide classes seemed to be similar.

Record Date Created: 19870626

Record Date Completed: 19870626

5/7/219 (Item 58 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07438455 PMID: 3577583

Repeatability of C-peptide response in **glucagon** stimulation test.

Sarlund H; Siitonen O; Laakso M; Pyorala K

Acta endocrinologica (DENMARK) Apr **1987**, 114 (4) p515-8, ISSN 0001-5598 Journal Code: 0370312

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Measurement of the plasma C-peptide level before and after iv administration of 1 mg of **glucagon** was repeated four times in 10 elderly non-diabetic subjects and in 20 elderly non-insulin-dependent diabetics **treated** with diet or oral drugs to assess the repeatability of the C-peptide responses. Plasma C-peptide levels before and after **glucagon** administration and C-peptide glucose ratios in the four measurements did not differ significantly from test to test either in diabetic or non-diabetic subjects. The results of the present study indicate that the repeatability of C-peptide response to **glucagon** is very good both in non-insulin-dependent diabetics and in non-diabetic subjects.

Record Date Created: 19870610

Record Date Completed: 19870610

5/7/220 (Item 59 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07425018 PMID: 2952663

Hyperglycemia and obesity as determinants of glucose, insulin, and **glucagon** responses to beta-endorphin in human **diabetes** mellitus.

Giugliano D; Salvatore T; Cozzolino D; Ceriello A; Torella R; D'Onofrio F

Journal of clinical endocrinology and metabolism (UNITED STATES) Jun **1987**, 64 (6) p1122-8, ISSN 0021-972X Journal Code: 0375362

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

The effect of human beta-endorphin on plasma glucose, insulin, and **glucagon** concentrations was studied in patients with noninsulin-dependent **diabetes** mellitus and in normal subjects. The

subjects were divided according to their body weight into lean (body mass index, less than 25) and obese (body mass index, greater than 29.5) groups. In lean subjects, infusion of 0.5 mg/h beta-endorphin caused significant increases in peripheral plasma glucose and **glucagon** levels, but no change in plasma insulin. In obese subjects, there was an immediate marked increase in both plasma insulin and **glucagon** concentrations during the beta-endorphin infusion, but the plasma glucose response was lower than that of lean subjects. In lean diabetic patients, beta-endorphin produced significant simultaneous increments in both insulin and **glucagon** concentrations and significantly decreased plasma glucose levels. These hormonal responses to beta-endorphin were amplified in the obese diabetic patients. There was a significant correlation (r = 0.61; P less than 0.01) between fasting plasma glucose levels and the integrated insulin area in response to beta-endorphin. The infusion of a lower dose of beta-endorphin (0.05 mg/h) in diabetic patients produced similar increments in both insulin and **glucagon** levels and also decreased plasma glucose concentration. These results indicate that beta-endorphin may have important glucoregulatory effects in man depending on the dose **administered** , the presence of obesity, and the prevailing plasma glucose concentration.

Record Date Created: 19870623

Record Date Completed: 19870623

5/7/221 (Item 60 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07337006 PMID: 3542595

Mechanism of the blunted **glucagon** response to insulin-induced hypoglycemia in diabetics]

Katsura M

Nippon Naibunpi Gakkai zasshi (JAPAN) Nov 20 **1986**, 62 (11) p1276-88, ISSN 0029-0661 Journal Code: 0413717

Document type: Journal Article ; English Abstract

Languages: JAPANESE

Main Citation Owner: NLM

Record type: Completed

It has been widely reported that dysfunctions of pancreatic A-cell occur in diabetics. Since these pancreatic A-cell dysfunctions are not normalized by conventional insulin injection **treatment**, they were thought to be a primary defect of **diabetes** mellitus. Recently it was found that paradoxic **glucagon** secretion to oral glucose and excessive **glucagon** response to i.v. arginine could be perfectly normalized if strict blood glucose regulations were achieved with appropriate insulin **treatment** . However, there has been no report on the perfect normalization of **glucagon** secretion in response to insulin-induced hypoglycemia in diabetics. In this report, to elucidate the precise significance of A-cell function in hypoglycemia in diabetics, the effect of long-term strict glycemic regulations and the importance of intact autonomic nerve function on hypoglycemia-induced **glucagon** secretion were studied. In experiments on hypoglycemia-induced **glucagon** secretion in diabetics, 0.2 to 0.3 U/kg of regular insulin injection were usually employed to overcome the hyperglycemia and insulin resistance. However, hyperinsulinemia has been demonstrated to suppress A-cell function in experiments using the euglycemic clamp technique. Therefore, the effect of plasma insulin concentrations after insulin injections was first studied in 7 healthy volunteers by injecting insulin at doses of 0.1 U/kg and 0.3 U/kg. In this experiment with 0.3 U/kg of insulin, the rate of fall in glycemia and the nadir of blood glucose were made similar to that with 0.1 U/kg of insulin by using glucose clamp technique with artificial endocrine pancreas. The plasma **glucagon** response after 0.3 U/kg of insulin was

significantly suppressed as compared to that after 0.1 U/kg of insulin. From these experiments, it was concluded that not only hypoglycemic stimuli but also plasma insulin concentrations are important factors for demonstrating significant **glucagon** secretion in response to insulin-induced hypoglycemia. Second, the effects of strict glycemic control and autonomic nerve function on hypoglycemia-induced **glucagon** secretion were studied. Regular insulin at a dose of 0.1 U/kg was injected in an i.v. bolus form into 21 insulin-dependent (IDDM) and 22 noninsulin-dependent (**NIDDM**) diabetics before and one to three months after strict glycemic control with multiple insulin injection therapy or continuous subcutaneous insulin infusion therapy. To reduce fasting blood glucose level and to obtain the same hypoglycemic stimuli, overnight insulin infusion at a basal dose was undertaken in IDDM who showed hyperglycemia before strict glycemic regulations.(ABSTRACT TRUNCATED AT 400 WORDS)

Record Date Created: 19870310
Record Date Completed: 19870310

5/7/222 (Item 61 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07298628 PMID: 3786296

[Urocanic acid content of the epidermis of diabetics]

Soderzhanie urokaninovoi kisloty v epidermise kozhi bol'nykh sakharnym diabetom.

Eremina I A; Mamaeva G G; Likhacheva N V; Burobin V A

Problemy endokrinologii (USSR) Sep-Oct **1986**, 32 (5) p15-8, ISSN 0375-9660 Journal Code: 0140673
Document type: Case Reports; Journal Article ; English Abstract
Languages: RUSSIAN
Main Citation Owner: NLM
Record type: Completed

A degree of a decrease in the content of urocanic acid in washes-off from the skin surface of patients with decompensated **diabetes** mellitus depends on a period and gravity of disease that may be indicative of disorders of the adenylate cyclase system (or one of its links). Change in the content of urocanic acid in the epidermis of patients with **diabetes** mellitus **treated** with the Biostator apparatus, correlates with change in the content of **glucagon** and blood sugar. The authors discuss a possibility to use the test of urocanic acid determination for the prediction and assessment of the efficacy of therapy of patients with **diabetes** mellitus.

Record Date Created: 19861229
Record Date Completed: 19861229

5/7/223 (Item 62 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07198082 PMID: 3526507 Record Identifier: 86288978

Diabetes, insulin and exercise.

Richter E A; Galbo H

Sports medicine (Auckland, N.Z.) (NEW ZEALAND) Jul-Aug **1986**, 3 (4) p275-88, ISSN 0112-1642 Journal Code: 8412297
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Other Citation Owner: NASA
Record type: Completed

The metabolic and hormonal adaptations to single exercise sessions and to exercise training in normal man and in patients with insulin-dependent as well as non-insulin-dependent **diabetes** mellitus are reviewed. In insulin-dependent (type I) **diabetes** good metabolic control is best obtained by a regular pattern of life which will lead to a fairly constant demand for insulin from day to day. Exercise is by nature a perturbation that makes **treatment** of **diabetes** difficult: Muscle contractions per se tend to decrease the plasma glucose concentration whereas the exercise-induced response of the so-called counter-regulatory hormones tend to increase plasma glucose by increasing hepatic glucose production and adipose tissue lipolysis. If the pre-exercise plasma insulin level is high, hypoglycaemia may develop during exercise whereas hyperglycaemia and ketosis may develop if pre-exercise plasma insulin levels are low. Physical activity is often difficult to carry out on a precise schedule and the exercise-induced changes in demand for insulin and calories vary according to the intensity and duration of exercise, time of day, and differ within and between individuals. Thus, physical training can not be recommended as a means of improving metabolic control in insulin-dependent **diabetes**. However, our present knowledge and technology allows the well-informed and cooperative patient to exercise and even to reach the elite level. To achieve this, pre-exercise metabolic control should be optimal and knowledge of the patient's reaction to exercise is desirable, which necessitates frequent self-monitoring of plasma glucose. It may often be necessary to diminish the insulin dose before exercise, and/or to ingest additional carbohydrate during or after exercise. In non-insulin-dependent (**type II**) **diabetes**, exercise is associated with less risk of metabolic derangement, and in genetically disposed individuals physical training may prevent development of overt **diabetes** possibly by diminishing the strain on the pancreatic beta cell. The latter, however, is only achieved if exercise is not accompanied by increased caloric intake. Whether physical training in **diabetes** can reduce cardiovascular morbidity and mortality is at present unknown, but training has in diabetic patients been shown to lessen some risk factors for development of arteriosclerosis. However, training of diabetics (especially in the less well-regulated patient) may not lessen coronary risk factors to the same extent as in healthy subjects. (118 Refs.)

Record Date Created: 19860925
Record Date Completed: 19860925

5/7/224 (Item 63 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07147720 PMID: 3012923

Impaired insulin secretion in human **diabetes** mellitus. Effect of pharmacological activation of gamma-aminobutyric acid system.

Quatraro A; Consoli G; Stante A; Minei A; Ceriello A; Passariello N; Giugliano D

Acta diabetologica latina (ITALY) Jan-Mar **1986**, 23 (1) p23-8,
ISSN 0001-5563 Journal Code: 0123567
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

To evaluate whether the gamma-aminobutyric acid (GABA)ergic system plays a role in the defective insulin secretion in human **diabetes** mellitus, 15 non-insulin-dependent diabetics with fasting hyperglycemia above 140 mg/dl were submitted to two consecutive i.v. glucose tolerance tests (IVGTT) (0.33 g/kg b.w.), in basal conditions and after pharmacologic activation of the GABA system with baclofen and sodium valproate. Baclofen, a synthetic analogue, was given to 8 diabetics in two divided doses of 10

mg each 8h and 1h before the post-**treatment** test; sodium valproate, a drug that increases endogenous GABA activity, was given orally (800 mg) 60 min before the performance of the post-**treatment** IVGTT. Neither **treatment** brought about significant changes in insulin, C-peptide, **glucagon** or growth hormone responses to i.v. glucose nor did they significantly change glucose disappearance rates. These results seem to indicate that GABA does not play a major role in the pathogenesis of defective insulin secretion in non-insulin-dependent **diabetes** mellitus.
Record Date Created: 19860707
Record Date Completed: 19860707

5/7/225 (Item 64 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07101706 PMID: 3516607
Secondary failure to **treatment** with oral antidiabetic agents in non-insulin-dependent **diabetes**.
Groop L C; Pelkonen R; Koskimies S; Bottazzo G F; Doniach D
Diabetes care (UNITED STATES) Mar-Apr **1986**, 9 (2) p129-33, ISSN 0149-5992 Journal Code: 7805975
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
To study the etiopathogenesis of secondary drug failure to **treatment** with oral antidiabetic agents in patients with non-insulin-dependent **diabetes** (NIDD) we compared 60 "nonresponders" with 60 "responders" to **treatment** with oral drugs. Secondary drug failure was defined as mean diurnal blood glucose greater than 12 mmol/L after an initial good response of greater than or equal to 2 yr. The nonresponders were characterized by 50% lower C-peptide concentrations than the responders (P less than 0.001). We could not, however, define a critical C-peptide level to discriminate between patients requiring and not requiring insulin therapy. There was a wide overlap of individual C-peptide values between responders and nonresponders that attenuates the clinical value of single C-peptide measurements in predicting therapy. Only by serial measurements over a period of time was it possible to achieve information about changes in beta cell function. The nonresponders showed increased frequency of islet cell (P less than 0.01), thyroid antimicrosomal (P less than 0.01), and gastric parietal cell antibodies (P less than 0.02). In nonresponders, HLA-antigen B8 was increased (P less than 0.05) and HLA-B7 decreased (P less than 0.01) compared with frequencies of responders. In conclusion, impaired beta cell function is a characteristic feature of many, but not all, NIDD patients who fail on **treatment** with oral antidiabetic drugs. The presence of islet cell and thyrogastric antibodies can unmask a distinct group of NIDD patients with a high risk of secondary drug failure and subsequent insulin dependency. HLA typing may further help to predict secondary failure in NIDD.
Record Date Created: 19860610
Record Date Completed: 19860610

5/7/226 (Item 65 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06993702 PMID: 3000857
Chlorpropamide raises fructose-2,6-bisphosphate concentration and

inhibits gluconeogenesis in isolated rat hepatocytes.
Monge L; Mojena M; Ortega J L; Samper B; Cabello M A; Feliu J E
Diabetes (UNITED STATES) Jan **1986**, 35 (1) p89-96, ISSN 0012-1797 Journal Code: 0372763
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The addition of chlorpropamide to hepatocytes isolated from fed rats raised the cellular concentration of fructose-2,6-bisphosphate (F-2,6-P2), a regulatory metabolite that plays a relevant role in the control of hepatic glucose metabolism. The effect of chlorpropamide was dose dependent; a statistically significant increase was already seen at 0.2 mM of the sulfonylurea. The accumulation of F-2,6-P2 caused by chlorpropamide (1 mM) was parallel to the stimulation of L-lactate production (36.6 +/- 4.8 versus 26.1 +/- 2.6 mumol of lactate/g of cells X 20 min; N = 5, P less than 0.05) and to the inhibition of gluconeogenesis (0.57 +/- 0.1 versus 0.94 +/- 0.09 mumol of [U-14C]pyruvate converted to glucose/g of cells X 20 min; N = 5, P less than 0.05). In addition, chlorpropamide enhanced the inhibitory action evoked by insulin on **glucagon** -stimulated gluconeogenesis. This combined effect of chlorpropamide and insulin seems to be correlated with the synergistic accumulation of F-2,6-P2 provoked by the simultaneous action of these two agents on **glucagon-treated** hepatocytes. Finally, neither 6-phosphofructo-2-kinase activity nor hepatocyte cyclic AMP levels were significantly changed by the presence of the sulfonylurea in the incubation medium. Our results support the concept that chlorpropamide, by a cyclic AMP-independent mechanism, increases the hepatic content of F-2,6-P2 and, in this way, enhances the glycolytic flux and inhibits glucose output by the liver.
Record Date Created: 19860124
Record Date Completed: 19860124

5/7/227 (Item 66 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06981152 PMID: 3906851
C-peptide determination in the choice of **treatment** in **diabetes** mellitus.
Koskinen P; Viikari J; Irjala K; Kaihola H L; Seppala P
Scandinavian journal of clinical and laboratory investigation (NORWAY) Nov **1985**, 45 (7) p589-97, ISSN 0036-5513 Journal Code: 0404375
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The predictive value of the intravenous **glucagon** test in assessing the requirement of insulin therapy in **diabetes** mellitus was evaluated in 105 adult diabetics. Basal and stimulated C-peptide concentrations and increments of C-peptide concentration were examined separately among newly and previously diagnosed diabetics. The poststimulatory C-peptide concentration of 0.6 nmol/l (Novo, antibody M 1230) proved to be the most reliable basis for the choice of therapy. Adequate therapy could have been assessed in 70 cases (67%) without **glucagon** stimulation. To derive maximal information of plasma C-peptide concentrations, a biphasic scheme of the use for C-peptide determinations and **glucagon** stimulation is presented. Basal and stimulated C-peptide levels of insulin-requiring diabetics correlated negatively with the duration of **diabetes** but they did not correlate with the relative body weights. Basal and stimulated C-peptide levels of non-insulin-requiring diabetics did not correlate with the duration of **diabetes** , but they correlated positively with the

relative body weights.
Record Date Created: 19860121
Record Date Completed: 19860121

5/7/228 (Item 67 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06908945 PMID: 3898764
New probes to study insulin resistance in men; futile cycle and glucose turnover.
Vranic M; Wajngot A; Efendic S
Advances in experimental medicine and biology (UNITED STATES) **1985,** 189 p227-45, ISSN 0065-2598 Journal Code: 0121103
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Insulin resistance has been measured in man by nonsteady state tracer methodology. Increase in overall glucose utilization and suppression of glucose production was measured when hyperglycemia was achieved either by infusing **glucagon** or glucose. With the first method, insulin resistance was assessed in obese man and in lean hypertriglyceridemic patients. With the second method, insulin resistance was assessed in lean mild **type II** diabetics. These methodologies can only assess deficiences in overall glucose utilization and glucose production, but cannot delineate the defect in glucose uptake by the liver. However, if a given metabolic event is essentially characteristic of only one organ, metabolic abnormalities specific to that organ can be detected **in vivo** provided there is a probe specific to that metabolic pathway. Therefore, in lean mild **type II** diabetics the liver glucose futile cycle was assessed by a double tracer method. Previously it was shown that liver glucose futile cycling is increased in diabetic dogs. In healthy control subjects in basal state and during glucose infusion, the futile cycle could not be detected, but it represented a major part of glucose metabolism in liver of **type II** diabetics. It appears, therefore, that most of the glucose taken up by the liver during the glucose challenge in diabetics reenters the blood stream without being oxidized or polymerized. On the basis of these studies, it was concluded that excessive hyperglycemia in the diabetics during glucose infusion is due to a decrease in irreversible glucose uptake (impaired phosphorylation and futile cycling) and to a decrease in suppression of glucose production. The relative contribution of the liver and periphery to hyperglycemia seems to be almost equivalent. The mechanism behind the increased glucose cycle activity is not clear. It may be due to a relative decrease of glycogen synthase or increase in glucose-6-phosphatase or both. These observations in mild lean **type II** diabetics may have implications also in some other types of **diabetes** , since we have observed that futile cycling is even more marked in obese **type II** diabetics and that it could account in part for the diabetogenic effect of growth hormone in acromegalics.
Record Date Created: 19851024
Record Date Completed: 19851024

5/7/229 (Item 68 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06908944 PMID: 4036714
Insulin-mediated and non-insulin-mediated metabolic effects of

gastroenteropancreatic peptides in type I and **type II diabetes**.
Dupre J; Baer A; Lee M; McDonald T J; Radziuk J; Rodger N W; Sullivan S
Advances in experimental medicine and biology (UNITED STATES) **1985**, 189 p207-25, ISSN 0065-2598 Journal Code: 0121103
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In this brief review of regulatory function of gastroenteropancreatic peptides in control of intermediary metabolism in normal and diabetic states, with and without mediation by insulin and/or **glucagon**, a variety of possible mechanisms have been described. It is apparent that the pharmacologic actions of the peptides identified in various locations provide models for multiple routes of delivery and modes of action of effectors in this control system. Examples already exist of each of the hypothetical mechanisms illustrated in the scheme in Figure 4. It is clear that a great deal of study will be necessary in identification of the active agents and assessment of their importance in the physiology of intermediary metabolism. With respect to the possible pathophysiologic roles of regulatory peptides of the gastroenteropancreatic system other than insulin and **glucagon**, a number of considerations of Type I and **Type II diabetes** have been raised. The balance of the evidence suggests that Type I **diabetes** may be viewed as an insulin deficiency syndrome, so that physiological replacement with insulin may be expected to result in correction of the metabolic abnormalities. Nevertheless, the difficulty of physiologic replacement **treatment**, which may call for portal delivery of insulin, is well recognized, and abnormalities secondary to insulin deficiency even in "well-**treated**" Type I **diabetes** may be compounded by the effects of gastroenteropancreatic peptides other than insulin, exerted through the various mechanisms discussed. In **Type II diabetes** mellitus, current understanding of the pathophysiology is much less complete and no convincing description of the etiology exists. The various metabolic actions of the gastroenteropancreatic peptides, and their interactions with other endocrine, paracrine and nervous regulatory mechanisms, represent a dauntingly complex control system. The elucidation of this system can provide fertile ground for the development and testing of hypotheses for the pathophysiology of disordered metabolism in **Type II diabetes** mellitus.
Record Date Created: 19851024
Record Date Completed: 19851024

5/7/230 (Item 69 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06891402 PMID: 3896885
[Effects of nifedipine on carbohydrate metabolism in the non-insulin dependent diabetic]
Effects de la nifedipine sur le metabolisme hydrocarbone chez le diabetique non insulino-dependant.
Abadie E; Villette J M; Gauville C; Tabuteau F; Fiet J; Passa P
Diabete & metabolisme (FRANCE) Jun **1985**, 11 (3) p141-6, ISSN 0338-1684 Journal Code: 7604157
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial ; English Abstract
Languages: FRENCH
Main Citation Owner: NLM
Record type: Completed
The aim of this prospective, randomized, double-blind, placebo controlled

study was to investigate the effect of nifedipine on carbohydrate metabolism in diabetic patients after a 3-day and a 3-month course of **treatment** . Sixteen non obese, well controlled non-insulin dependent diabetics, (HbA1 less than 10%), with moderate untreated hypertension were divided in two groups: nifedipine (group N, 8 patients) and placebo (group P, 8 patients). An oral glucose tolerance test (OGTT, 75 g glucose) and an arginine infusion were performed before, after a 3-day, and a 3-month course, either of nifedipine 30 mg/D or placebo. Blood samples obtained during OGTT were assayed for glucose and insulin, and during arginine infusion for insulin, **glucagon** and growth hormone. The differences between basal and peak values during tests were compared between both groups before and after **treatment** using Wilcoxon's rank sum test. Neither acute nor chronic administration of nifedipine or placebo modified the glucose tolerance. However, basal insulin levels were reduced by 3 month-administration of nifedipine (from 19 +/- 2 micromicrons/ml to 10 +/- 1 micromicrons/ml, p = 0,01). Otherwise the basal and peak hormonal values during tests were not significantly affected by nifedipine either at the start of after 3 months of **treatment**. These results suggest that nifedipine, when given in standard dosage for 3 months, has minor effects on carbohydrate metabolism in non-insulin dependent diabetic patients.

Record Date Created: 19851007
Record Date Completed: 19851007

5/7/231 (Item 70 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06726706 PMID: 6395671

Diabetes mellitus: relationships of nonhuman primates and other animal models to human forms of **diabetes**.

Howard C F

Advances in veterinary science and comparative medicine (UNITED STATES) **1984**, 28 p115-49, ISSN 0065-3519 Journal Code: 0216540
Contract/Grant No.: RR-00163; RR; NCRR; RR-00165; RR; NCRR; RR-05694; RR; NCRR; +
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Results from studies with M. nigra allow some conclusions and predictions about the etiology and development of **diabetes** relative to the islet lesion in monkeys and human beings. Some factor or factors must initiate the lesion; whether this is genetic, environmental, or a combination of both is not known. Amyloid is not the initiating factor to the islet lesion, but appears later as there is deterioration of cells. Sufficient evidence does not yet exist to choose from among the alternatives regarding the source of amyloid. With gradual deterioration of cells and replacement by amyloid, secretion of insulin is impaired and concentrations of **glucagon** increase. Sufficient circulating insulin is probably chronically available to the cells in this moderately impaired state, so that an acute decrease in delta IRI in response to glucose in an iv-**administered** GTT does not cause significant impairment in glucose clearance. The increase in circulating **glucagon** is probably due to a loss of controls on alpha-cell secretion or synthesis of **glucagon**. Fasting glucose levels increase but remain within the nondiabetic range. Eventually there is sufficient accretion of amyloid, usually greater than 50%, so that substantial beta-cell loss occurs and the monkey can no longer maintain fasting normoglycemia. The monkey then is hyperglycemic and hypoinsulinemic. Only at this time are the impairments detectable by the usual diagnostic clinical criterion of hyperglycemia. The ICAs arise in response to secretory cell deterioration and are present until there no

longer are sufficient cells to elicit an immune response. Results from M. nigra can give insight into a similar condition that probably exists in a subpopulation of older diabetic humans. Humans probably pass through stages similar to those discerned in monkeys. Nondiabetic humans with sufficient beta cells to sustain adequate secretion of insulin, but with moderate amyloid infiltration, probably would be in a category equivalent to BD monkeys; since these people are not overtly hyperglycemic, they are not clinically recognizable as diabetic and would be classified retrospectively as nondiabetic. Continued loss of cells with concomitant amyloid deposition would eventually lead to hyperglycemia; if examined at autopsy, these people would have visible islet amyloid as well as a retrospective diagnosis of **diabetes**. Older **type II** diabetic humans with ICA usually proceed to insulin therapy more rapidly than do those who are ICA negative (Irvine et al., 1977; Del Prete et al., 1977; Gray et al., 1980).(ABSTRACT TRUNCATED AT 400 WORDS) (327 Refs.)
Record Date Created: 19850228
Record Date Completed: 19850228

5/7/232 (Item 71 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06723961 PMID: 6151747
New pharmacologic approaches to the **treatment** of **diabetes**.
Johnson D G; Bressler R
Special topics in endocrinology and metabolism (UNITED STATES) **1984**, 6 p163-92, ISSN 0193-0982 Journal Code: 8001537
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
(128 Refs.)
Record Date Created: 19850306
Record Date Completed: 19850306

5/7/233 (Item 72 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06673215 PMID: 6390424
Hormonal function of islands of Langerhans in **diabetes** mellitus]
Gormonal'naia funktsiia ostrovkovogo apparata podzheludochnoi zhelezy pri sakharnom diabete.
Balabolkin M I; Abrikosova S Iu
Problemy endokrinologii (USSR) Sep-Oct **1984**, 30 (5) p16-8, ISSN 0375-9660 Journal Code: 0140673
Document type: Journal Article ; English Abstract
Languages: RUSSIAN
Main Citation Owner: NLM
Record type: Completed
Some hormonal characteristics were examined in 23 patients with **diabetes** mellitus. Of these, 7 patients had an insulin-dependent and 19 an insulin-independent disease pattern. It was demonstrated that after **treatment** the level of IRI and c-peptide remained within normal. The levels of **glucagon** and somatostatin were considerably elevated and did not show any noticeable decrease after **treatment**. Both groups manifested an increased number of antibodies against insulin, with that number remaining virtually unchanged after **treatment**.
Record Date Created: 19850118
Record Date Completed: 19850118

5/7/234 (Item 73 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06673213 PMID: 6390423
Levels of various pituitary and pancreatic hormones in the blood of patients with non-insulin-dependent **diabetes** mellitus]
Uroven' nekotorykh gormonov gipofiza i podzheludochnoi zhelezy v krovi bol'nykh insulinonezavisimym sakharnym diabetom.
Perelygina A A; Golikova A A; Zin'ko N V
Problemy endokrinologii (USSR) Sep-Oct **1984**, 30 (5) p10-3, ISSN 0375-9660 Journal Code: 0140673
Document type: Journal Article ; English Abstract
Languages: RUSSIAN
Main Citation Owner: NLM
Record type: Completed
The level of pituitary hormones (somatotropin and prolactin) and pancreatic hormones (insulin and **glucagon**) was measured by radioimmunoassay in blood of patients with insulin-independent **diabetes** mellitus with and without diabetic microangiopathies, in the state of decompensation and during **treatment**. Forty-four patients aged 26 to 60 years were examined. Some patients with insulin-independent **diabetes** with and without diabetic microangiopathies demonstrated an elevation of blood insulin and **glucagon**. The blood somatotropin level was found to be increased in patients with insulin-independent **diabetes** mellitus with diabetic microangiopathies in the state of decompensation. No correlations were established between prolactin and insulin levels, somatotropin and insulin levels in the blood of patients with insulin-independent **diabetes** mellitus. During **treatment**, one could see a decrease in the somatotropin content and a tendency toward elevation in the insulin content and reduction in the **glucagon** level in patients with insulin-independent **diabetes** with diabetic microangiopathies.
Record Date Created: 19850118
Record Date Completed: 19850118

5/7/235 (Item 74 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06661308 PMID: 6437842
Glibenclamide pharmacokinetics in acarbose-**treated type 2** diabetics.
Gerard J; Lefebvre P J; Luyckx A S
European journal of clinical pharmacology (GERMANY, WEST) **1984**, 27 (2) p233-6, ISSN 0031-6970 Journal Code: 1256165
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
A single dose of glibenclamide 5 mg was **administered** to six **Type 2** diabetics, randomly **treated** for 7 days either with acarbose (3 X 100 mg daily) or with placebo. The serum concentration of the drug was measured for 10 h. Peak concentrations, times-to-peak concentration, elimination half-lives and the extent of bioavailability of the drug were not significantly modified by acarbose. The combined administration of glibenclamide and acarbose resulted in a modest improvement in the blood glucose profile after breakfast and lunch,

together with a significant diminution in plasma insulin. Thus, acarbose appears a useful additional **treatment** for **Type 2** diabetics already receiving sulphonylurea derivatives.
Record Date Created: 19841226
Record Date Completed: 19841226

5/7/236 (Item 75 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06656784 PMID: 6388587
Lack of relationship between plasma insulin and **glucagon** levels and angiographically-documented coronary atherosclerosis.
Mookherjee S; Potts J L; Hill N E; Warner R; Raheja K L; Patel D G; Vardan S; Smulyan H
Atherosclerosis (NETHERLANDS) Oct **1984**, 53 (1) p99-109, ISSN 0021-9150 Journal Code: 0242543
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In 120 consecutive patients undergoing diagnostic coronary arteriography, fasting blood glucose, plasma insulin, **glucagon**, serum cholesterol and triglyceride concentrations were measured. The insulin-glucose ratio and insulin-**glucagon** ratio were calculated. Forty-five patients had normal coronary arteries, 19 had single vessel coronary artery disease and 56 patients had multiple vessel disease. Fasting blood glucose was greater than 120 mg/100 ml in 37 patients (group A) and included 9 of the 10 known diabetics, 3 of whom were being **treated** with insulin. Seventy-seven patients included in group B had fasting blood glucose concentration less than 120 mg/100 ml. Patients with multiple vessel coronary disease in either group had higher blood glucose and cholesterol concentrations than those with normal coronary arteries or the ones with single vessel disease, but they did not have higher plasma insulin or **glucagon** levels nor increased insulin-glucose or insulin-**glucagon** ratios. With comparable extent of coronary artery disease patients in group A had higher plasma insulin levels and insulin-**glucagon** ratios than those in group B, but no correlation exists between the presence or extent of coronary atherosclerosis and these variables in either group. Thus, neither fasting plasma insulin level nor insulin-**glucagon** ratio predicts the status of underlying coronary atherosclerosis in either diabetics or nondiabetics.
Record Date Created: 19841219
Record Date Completed: 19841219

5/7/237 (Item 76 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06607431 PMID: 6433609
Biochemical characterization of ketosis-resistant young diabetics of northern India. **In vivo** effects of i.v. glucose, s.c. epinephrine and i.v. **glucagon** and in vitro effects of anti-insulin serum on adipose tissue lipolysis.
Krishna Ram B; Sachdev G; Chopra A; Karmarkar M G
Acta diabetologica latina (ITALY) Apr-Jun **1984**, 21 (2) p141-51, ISSN 0001-5563 Journal Code: 0123567
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Epinephrine (10 micrograms/kg body weight) s.c., **glucagon** (1 microgram/kg body weight) i.v. and glucose (0.5 g/kg body weight) i.v. were injected in groups of ketosis-prone young diabetics, ketosis-resistant young diabetics, maturity-onset diabetics, young and mature controls, each group comprising 8 subjects. Samples were drawn at timed intervals and analyzed for glucose, FFA, acetone, citrate and plasma free insulin. FFA and glycerol release by the adipose tissue in vitro was studied in 6 of each of the following groups: young diabetics and young controls in the presence of norepinephrine, anti-insulin serum or both. Failure of the adipose tissue of ketosis-resistant young diabetics to respond to lipolytic and ketogenic hormones has been suggested by others as the basis for the clinically observed resistance to ketoacidosis. The present data do not confirm any failure of the liver or adipose tissue to respond to **glucagon** , epinephrine or norepinephrine in these diabetics. The ketosis-resistant young diabetics have some endogenous insulin secretory capacity still preserved as evident from their basal and post-glucose free insulin levels and effects of anti-insulin serum on in vitro lipolysis by their adipose tissues. The available endogenous insulin though adequate in preventing excessive lipolysis and ketogenesis, appears insufficient to check hyperglycemia.

Record Date Created: 19840921

Record Date Completed: 19840921

5/7/238 (Item 77 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

06525229 PMID: 6373812

Gastric inhibitory polypeptide in obesity and **diabetes** mellitus.

Service F J; Rizza R A; Westland R E; Hall L D; Gerich J E; Go V L

Journal of clinical endocrinology and metabolism (UNITED STATES) Jun **1984**, 58 (6) p1133-40, ISSN 0021-972X Journal Code: 0375362

Contract/Grant No.: AM-20411; AM; NIADDK; AM-20973; AM; NIADDK; AM-29953; AM; NIADDK; +

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Gastric inhibitory polypeptide (GIP) concentrations may be influenced by obesity, **diabetes**, and **glucagon** deficiency and be under feedback inhibition by insulin. To assess these factors, insulin-dependent diabetic, totally pancreatectomized diabetic, and lean and obese noninsulin-dependent diabetic patients were studied twice, once during partial insulin withdrawal and again when euglycemia was achieved before and after mixed meal ingestion, using an artificial endocrine pancreas. The results were compared to those from weight-matched lean and obese nondiabetic subjects. No significant differences in postprandial GIP responses were found between lean and obese nondiabetic subjects. Despite basal and postprandial hyperglycemia, the GIP responses to the mixed meal were not significantly different between insulin-deficient (insulin-dependent and totally pancreatectomized) patients and lean nondiabetic subjects. In addition, there were no significant differences in postprandial GIP responses between insulin-dependent and totally pancreatectomized patients. In contrast, lean and obese noninsulin-dependent diabetic patients had reduced GIP responses compared to weight-matched nondiabetic subjects (mean +/- SE, 37.9 +/- 5.4 vs. 67.1 +/- 10.8 ng ml-1 240 min-1, respectively; P less than 0.05). This difference was entirely due to the reduced GIP responses in obese noninsulin-dependent diabetic patients compared to those in obese nondiabetic subjects (32.1 +/- 7.9 vs. 76.9 +/- 18.2 ng ml-1 240 min-1, respectively; P less than 0.05); the postprandial GIP responses were not

significantly different between lean noninsulin-dependent diabetic patients and lean nondiabetic subjects. Insulin infusion by an artificial endocrine pancreas resulted in postprandial insulin and glucose profiles that approximated those of nondiabetics, but did not significantly alter GIP responses to the mixed meal (48.2 +/- 5.5 ng ml-1 240 min-1) in the 18 diabetic patients compared to results obtained with sc insulin **treatment** (42.2 +/- 5.2 ng ml-1 240 min-1). In conclusion, postprandial GIP responses are normal in obese nondiabetic subjects and insulin-deficient diabetic patients and are blunted in obese, but not in lean, noninsulin-dependent diabetic patients. In addition, GIP does not appear to be under feedback inhibition by insulin or influenced by **glucagon** deficiency in **diabetes**.

Record Date Created: 19840702

Record Date Completed: 19840702

5/7/239 (Item 78 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

06522021 PMID: 6724097

Glucagon secretion in rats with non-insulin-dependent **diabetes**: an **in vivo** and in vitro study.

Giroix M H; Portha B; Kergoat M; Picon L

Diabete & metabolisme (FRANCE) Jan **1984**, 10 (1) p12-7, ISSN 0338-1684 Journal Code: 7604157

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Non-insulin-dependent **diabetes** (NIDD) was obtained in adult rats following a neonatal streptozotocin injection. Rats with NIDD exhibited a chronic low-insulin response to glucose **in vivo**, slightly elevated basal plasma glucose values (less than 2 g/l) and low pancreatic insulin stores (50% of the controls). **Glucagon** secretion was studied in this model, **in vivo** and in vitro using the isolated perfused pancreas technique. Normal basal plasma **glucagon** levels were observed in the fed state and were in accordance with normal basal **glucagon** release in vitro. The pancreatic **glucagon** stores were normal in the diabetics. In experiments with the perfused pancreas, the increased glucose concentration suppressed **glucagon** release as readily in the diabetics as in the controls. Moreover 5.5 mM glucose suppressed **glucagon** release stimulated by 19 mM arginine to the same extent in both groups. These data indicate that the suppression of A cell function by glucose is normal in rats with NIDD . Theophylline and isoproterenol also produced normal **glucagon** release in diabetics. By contrast, the **glucagon** secretion in response to arginine was lower in the diabetics. This was observed either **in vivo** (arginine infusion) or in vitro in the presence or the absence of glucose in the perfusate. But in the presence of theophylline the response to arginine was normalized in the diabetics. Impairment of A cell function of the diabetics is not limited to recognition of amino-acids, since acetylcholine evoked a lower **glucagon** response in the diabetics than in the controls. These defects are different from those described in their B cells.

Record Date Created: 19840713

Record Date Completed: 19840713

5/7/240 (Item 79 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

06520199 PMID: 6373160
Effect of middle-term gliclazide **treatment** on insulin secretion in non-insulin dependent diabetics.
Brogard J M; Pinget M; Dorner M
Current medical research and opinion (ENGLAND) **1984**, 9 (1) p56-63, ISSN 0300-7995 Journal Code: 0351014
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Insulin secretion was studied in 12 non-insulin dependent diabetics during middle-term administration of the sulphonylurea gliclazide. Blood sugar, C-peptide and **glucagon** were also estimated during the intravenous glucose tolerance and arginine tests performed before and after therapy. After 3 months of gliclazide therapy (240 mg/day) in addition to a low carbohydrate diet, the intravenous glucose tolerance test showed a significant reduction in blood sugar levels and in the partial and total areas under the blood sugar curve, as well as an improvement in early insulin secretion, characterized by a significant increase in plasma C-peptide at 4, 10 and 20 minutes. Plasma **glucagon** levels were not affected by the sulphonylurea therapy. In the arginine test, blood sugar levels were lower at the end of the **treatment** period; plasma insulin, C-peptide and **glucagon** did not change significantly. In this study, plasma C-peptide has proved to be a better indicator of stimulated insulin secretion than plasma insulin levels. The scarcity of hypoglycaemic episodes during therapy with gliclazide may be related to the selective stimulation of early insulin secretion by this drug.
Record Date Created: 19840719
Record Date Completed: 19840719

5/7/241 (Item 80 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06379451 PMID: 6148037
Metabolic effects of sulfonylurea drugs. A review.
Groop L
Annals of clinical research (FINLAND) **1983**, 15 Suppl 37 p16-20, ISSN 0003-4762 Journal Code: 0220042
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Although sulfonylureas have been used in the **treatment** of **type 2 diabetes** for more than 25 years, their mode of action is still largely unresolved. A number of pancreatic and extrapancreatic effects have been invoked to explain the hypoglycemic action of the drugs. It seems established that sulfonylureas enhance insulin secretion during short- and, possibly, also during long-term therapy, but differences between the various drugs are possible. Preserved beta-cell function is, however, a prerequisite for the blood glucose-lowering effects of these drugs. Among these, suppression of hepatic glucose production and enhancement of peripheral insulin sensitivity are clinically the most important. Reported effects relating to other hormones have proved difficult to confirm, and can often be explained by simultaneous changes in insulin secretion. Recent data provide evidence that sulfonylureas may differ in their metabolic effects. However, it remains to be determined, whether the differences are real or a consequence of different pharmacokinetics. (27 Refs.)
Record Date Created: 19840925
Record Date Completed: 19840925

5/7/242 (Item 81 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06364121 PMID: 6369443
Mechanism of action of sulfonylureas at the pancreatic and extra-pancreatic levels in prolonged **treatment** in noninsulin-dependent diabetic patients]
Mecanismo de accion en tratamientos prolongados a nivel pancreatico y extrapancreatico de las sulfonilureas en pacientes diabeticos no-insulindependientes.
Serrano Rios M; Ordonez Perez A J; Sanchez Arriaran M S; Villalba Diaz M T; Nash Raina R E; de la Vina S
Revista clinica espanola (SPAIN) Dec 31 **1983**, 171 (6) p385-90, ISSN 0014-2565 Journal Code: 8608576
Document type: Journal Article ; English Abstract
Languages: SPANISH
Main Citation Owner: NLM
Record type: Completed
Record Date Created: 19840523
Record Date Completed: 19840523

5/7/243 (Item 82 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05243017 PMID: 395094
Influence of insulin infusion kinetics of an artificial beta cell on blood glucose control in insulin-dependent diabetics.
Kerner W; Beischer W; Maier V; Pfeiffer E F
Hormone and metabolic research. Supplement series (GERMANY, WEST) **1979**, (8) p71-80, ISSN 0170-5903 Journal Code: 0330417
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The influence of different control modes for insulin infusion with an artificial beta cell was examined in 41 insulin-dependent diabetics. In 21 Patients, oral glucose tolerance tests were performed with control modes characterized either by low dynamic and high static gain (type I, 10 patients) or high dynamic and low static gain (type III, 11 patients). The change from type I to type III control mode effected an increase of initial insulin infusion rates (91 +/- 59 to 313 +/- 81 mU/min 10-20 min after glucose ingestion) and a decrease of infusion rates during the following phase of the 3-hour observation period (28.2 +/- 4.2 to 18.1 +/- 2.8 U) in patients whose blood glucose curves were completely normalized. Suppression of plasma **glucagon** levels, observed in 5 healthy control subjects, was not fully restored to normal in these patients. In another 20 insulin-dependent diabetics, daily insulin requirements form the artificial beta cell were determined by employing two control modes (types II and III) comparable in static control but different in dynamic control. Gain of dynamic control, especially in the range of falling glucose levels, was higher in type III control mode (15 patients) than in **type II** mode (5 patients). These insulin requirements were compared to the insulin doses necessary for subcutaneous **treatment**. While intravenous insulin requirements were much higher when **type II** control mode was employed (78.2 +/- 10.2%), during application of type III mode, intravenous insulin requirements were only 10.8 +/- 5.5% higher than subcutaneous doses. We conclude from these data that early increases in insulin infusion

rates followed by a rapid decrease seem to reduce insulin requirements after glucose ingestion. A high-gain dynamic control is the basis for this insulin infusion profile.
Record Date Created: 19800523
Record Date Completed: 19800523

5/7/244 (Item 83 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02020904 PMID: 12085573
Accelerated insulin degradation: an alternate mechanism for insulin resistance.
Kitabchi A E; Stentz F B; Cole C; Duckworth W C
Departments of Medicine and Biochemistry and the Clinical Research Center, University of Tennessee Center for the Health Sciences and Veterans Administration Hospital, Memphis, Tennessee, USA.
Diabetes care (United States) Nov-Dec **1979**, 2 (6) p414-7, ISSN 0149-5992 Journal Code: 7805975
Contract/Grant No.: AM 00187; AM; NIADDK; AM 07088; AM; NIADDK; GRRR05423 ; RR; NCRR; RR02211; RR; NCRR
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We have examined insulin and **glucagon** degrading activities of muscle and fat tissues in 11 subjects (4 lean controls, 3 insulin-resistant obese subjects, 2 non-insulin-dependent diabetic subjects, and 2 insulin-**treated** diabetic subjects) and correlated degrading activity with (1) basal insulin level and (2) state of insulin resistance. We found hyperinsulinemia and insulin resistance to be significantly correlated with accelerated insulin and **glucagon** degrading activity. Weight reduction in an insulin-resistant obese patient results in parallel reduction in both basal insulin level and insulin-**glucagon** degrading activity. These data are consistent with the hypothesis that an alternative mechanism for insulin resistance may be an accelerated insulin degradation at the level of target tissues.
Record Date Created: 20020627
Record Date Completed: 20020724

5/7/245 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

116035159 CA: 116(5)35159z PATENT
Glucagon-like peptide-1 (Glp-1) analogs useful for diabetes treatment
INVENTOR(AUTHOR): Buckley, Douglas I.; Habener, Joel F.; Mallory, Joanne B.; Mojsov, Svetlana
LOCATION: USA
PATENT: PCT International ; WO 9111457 A1 DATE: 910808
APPLICATION: WO 91US500 (910124) *US 468736 (900124)
PAGES: 50 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C07K-007/34A; C07K-007/10B; A61K-037/02B; A61K-037/28B DESIGNATED COUNTRIES: CA; JP; US
DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LU; NL; SE
SECTION:
CA202006 Mammalian Hormones
IDENTIFIERS: glucagon like peptide analog diabetes
DESCRIPTORS:
Antidiabetics and Hypoglycemics...
glucagon-like peptide-1 analogs as, for type II diabetes treatment

Peptides,uses...
    glucagon-like peptide-2 analogs, for type II diabetes treatment
Molecular structure-biological activity relationship...
    of glucagon-like peptide-1 analogs, insulin stimulation and diabetes type II treatment in relation to
Protein sequences...
    of glucagon-like peptide-2 analogs
  CAS REGISTRY NUMBERS:
9004-10-8 biological studies, stimulation of, glucagon-like peptide-1 analogs for, for diabetes type II treatment
106612-94-6 107444-51-9 119637-73-9 123475-27-4 123475-28-5 127650-06-0 138324-89-7 138324-90-0 138324-91-1 138324-92-2 138324-93-3 138324-94-4 138324-95-5 138324-96-6 138324-97-7 138324-98-8 138324-99-9 138325-00-5 138347-75-8 138347-76-9 for diabetes type II treatment
138347-77-0 glucagon-like peptide-1 analogs stability in relation to
138325-01-6 insulin-stimulating activity of, diabetes type II treatment in relation to

5/7/246 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

105188721 CA: 105(21)188721z JOURNAL
The Upjohn colony of KKAY mice: a model for obese type II diabetes
AUTHOR(S): Chang, A. Y.; Wyse, B. M.; Copeland, E. J.; Peterson, T.; Ledbetter, S. R.
LOCATION: Diabetes GI Dis. Res., Upjohn Co., Kalamazoo, MI, 49001, USA
JOURNAL: Int. Congr. Ser. - Excerpta Med. DATE: 1986 VOLUME: 700
NUMBER: Diabetes 1985 PAGES: 466-70 CODEN: EXMDA4 ISSN: 0531-5131
LANGUAGE: English
SECTION:
CA114008 Mammalian Pathological Biochemistry
CA101XXX Pharmacology
IDENTIFIERS: obesity diabetes mouse model pathophysiol, ciglitazone diabetes obesity mouse model
DESCRIPTORS:
Urine...
    albumin excess in, in obese type II diabetic mouse model
Animal respiration...
    by brown adipose tissue mitochondria, in obese type II diabetic mouse model
Obesity...
    diabetes mellitus type II-assocd., in KKAY mice, ciglitazone in relation to
Lipids,biological studies...
    formation of, from glucose by adipose tissue of obese type II diabetic mouse model
Blood plasma...
    glucagon and insulin of, in obese type II diabetic mouse model
Pancreatic islet of Langerhans...
    glucagon and insulin of, of obese type II diabetic mouse model
Adipose tissue,white,metabolism...
    glucose metab. by, in obese type II diabetic mouse model
Albumins,blood, metabolic disorders, hyperalbuminemia... Hyperglycemia...
    in diabetes mellitus obese type II model in KKaY mice
Appetite,disorder, hyperphagia...
    in diabetes mellitus obese type II mouse model, ciglitazone in relation to
Mouse...
    KKAY, as obese type II diabetes model, pathophysiol. of, ciglitazone

effect on
Adipose tissue,brown,metabolism...
mitochondrial protein of and respiration by, in obese type II diabetic mouse model
Diabetes mellitus,maturity-onset...
model for, pathophysiol. and ciglitazone treatment of, in KKAY mice
Proteins...
of brown adipose tissue mitochondria, in obese type II diabetic mouse model
Mitochondria...
proteins of and respiration by, in brown adipose tissue of obese type II diabetic mouse model
CAS REGISTRY NUMBERS:
50-99-7 biological studies, metab. of, by adipose tissue in obese type II diabetic mouse model
9004-10-8 9007-92-5 biological studies, of blood plasma and pancreas, in obese type II diabetic mouse model
74772-77-3 in diabetes mellitus obese type II treatment, in KAYy mice

5/7/247 (Item 1 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

09833458 Genuine Article#: CB015 Number of References: 27
Title: PERIODONTAL STATUS OF FINNISH ADOLESCENTS WITH INSULIN-DEPENDENT **DIABETES**-MELLITUS
Author(s): SANDHOLM L; SWANLJUNG O; RYTOMAA I; KAPRIO EA; MAENPAA J
Corporate Source: UNIV HELSINKI,DEPT PERIODONTOL,TOOLONTORINKATU 6A1/SF-00260 HELSINKI//FINLAND/; UNIV HELSINKI,DEPT CARDIOL/SF-00100 HELSINKI 10//FINLAND/; UNIV HELSINKI,CHILDRENS HOSP/SF-00100 HELSINKI 10//FINLAND/; AURORA HOSP/SF-00250 HELSINKI//FINLAND/
Journal: JOURNAL OF CLINICAL PERIODONTOLOGY, **1989**, V16, N10, P617-620
Language: ENGLISH Document Type: ARTICLE

5/7/248 (Item 2 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

09724884 Genuine Article#: AR124 Number of References: 16
Title: IMPAIRED SOMATOSTATIN RESPONSE TO ORALLY-**ADMINISTERED** GLUCOSE IN **TYPE-II DIABETES** ENTAILS BOTH SOMATOSTATIN-28 AND SOMATOSTATIN-14 AND IS ASSOCIATED WITH DERANGED METABOLIC CONTROL
Author(s): GUTNIAK M; GRILL V; ROOVETE A; EFENDIC S
Corporate Source: KAROLINSKA HOSP,DEPT ENDOCRINOL/S-10401 STOCKHOLM 60//SWEDEN/
Journal: ACTA ENDOCRINOLOGICA, **1989**, V121, N3, P322-326
Language: ENGLISH Document Type: ARTICLE

5/7/249 (Item 3 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

08618466 Genuine Article#: M1953 Number of References: 146
Title: PHARMACOLOGIC INTERVENTION IN **DIABETES**-MELLITUS
Author(s): MOHRBACHER RJ; KIORPES TC; BOWDEN CR
Corporate Source: MCNEIL PHARMACEUT,SPRING HOUSE/SPRING HOUSE//PA/19477
Journal: ANNUAL REPORTS IN MEDICINAL CHEMISTRY, **1987**, V22, P213-222
Language: ENGLISH Document Type: REVIEW, BIBLIOGRAPHY

5/7/250 (Item 4 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

08349457 Genuine Article#: K1927 Number of References: 21
Title: A STUDY OF BETA-CELL FUNCTION AFTER **GLUCAGON** STIMULATION IN THALASSEMIA MAJOR **TREATED** BY HIGH TRANSFUSION PROGRAM
Author(s): LIVADAS DP; ECONOMOU E; SOFRONIADOU K; FOTIADOUPAPPA H; VANMELLE GD; TEMLER E; FELBER JP
Corporate Source: CHU VAUDOIS,DIV ENDOCRINOL & BIOCHIM CLIN/CH-1011 LAUSANNE//SWITZERLAND/; VENIZELION GEN HOSP,ENDOCRINOL UNIT/HERAKLION CRETE//GREECE/; PIRAEUS GEN HOSP,CTR TRANSFUS/NIKEA PIRAEUS//GREECE/; UNIV LAUSANNE,SCH MED,IUMSP/CH-1005 LAUSANNE//SWITZERLAND/
Journal: CLINICAL ENDOCRINOLOGY, **1987**, V27, N4, P485-490
Language: ENGLISH Document Type: ARTICLE

5/7/251 (Item 5 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

08243373 Genuine Article#: J4226 Number of References: 21
Title: CORRELATIONS BETWEEN FASTING PLASMA C-PEPTIDE, **GLUCAGON** -STIMULATED PLASMA C-PEPTIDE, AND URINARY C-PEPTIDE IN INSULIN-**TREATED** DIABETICS
Author(s): GJESSING HJ; MATZEN LE; FROLAND A; FABER OK
Corporate Source: HORSHOLM HOSP,DEP MED/HORSHOLM//DENMARK/; FREDERICIA HOSP,DEPT MED/FREDERICIA//DENMARK/
Journal: DIABETES CARE, **1987**, V10, N4, P487-490
Language: ENGLISH Document Type: ARTICLE
? ds

Set	Items	Description
S1	5715	GLUCAGON AND (TYPE(W)2 OR TYPE(W)II OR NIDDM) AND DIABETES
S2	1360	S1 AND PY<1994
S3	765	RD S2 (unique items)
S4	293	S3 AND (TREAT? OR ADMINISTER? OR (IN(W)VIVO))
S5	251	S4 AND PY<1993

? ds

Set	Items	Description
S1	5715	GLUCAGON AND (TYPE(W)2 OR TYPE(W)II OR NIDDM) AND DIABETES
S2	1360	S1 AND PY<1994
S3	765	RD S2 (unique items)
S4	293	S3 AND (TREAT? OR ADMINISTER? OR (IN(W)VIVO))
S5	251	S4 AND PY<1993

?

---Logging off of Dialog---

? logoff
06sep04 14:34:24 User226352 Session D797.6
$30.34 5.418 DialUnits File5
$138.25 79 Type(s) in Format 7
$138.25 79 Types
$168.59 Estimated cost File5
$3.40 0.576 DialUnits File6
$3.40 Estimated cost File6
$84.12 4.103 DialUnits File34
$83.30 14 Type(s) in Format 7